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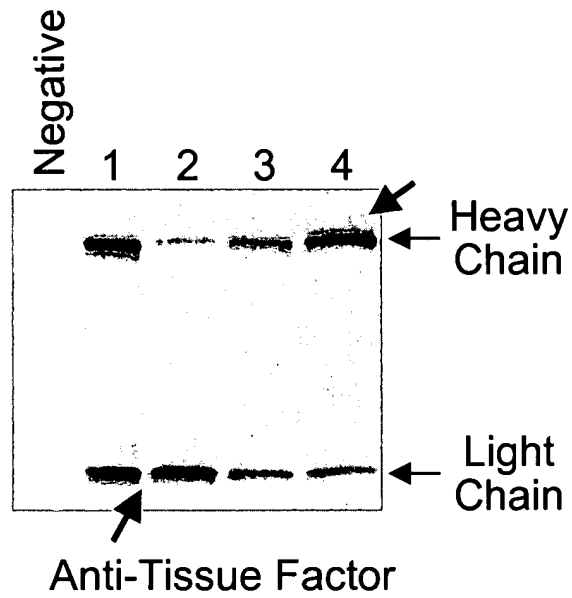
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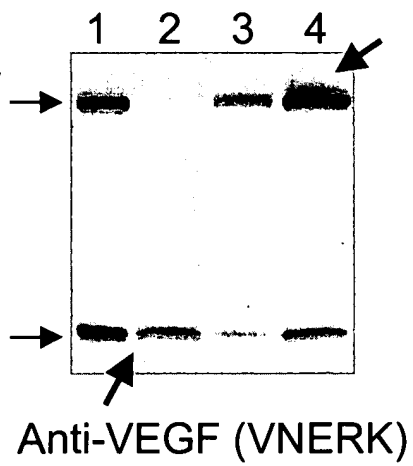
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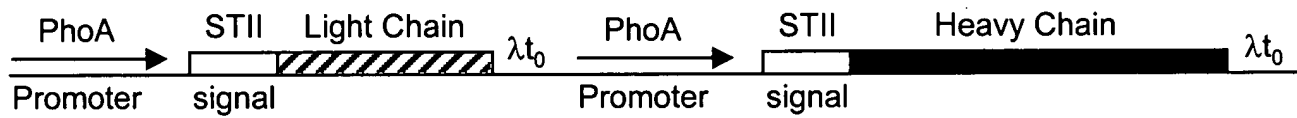
**Fig. 1A**



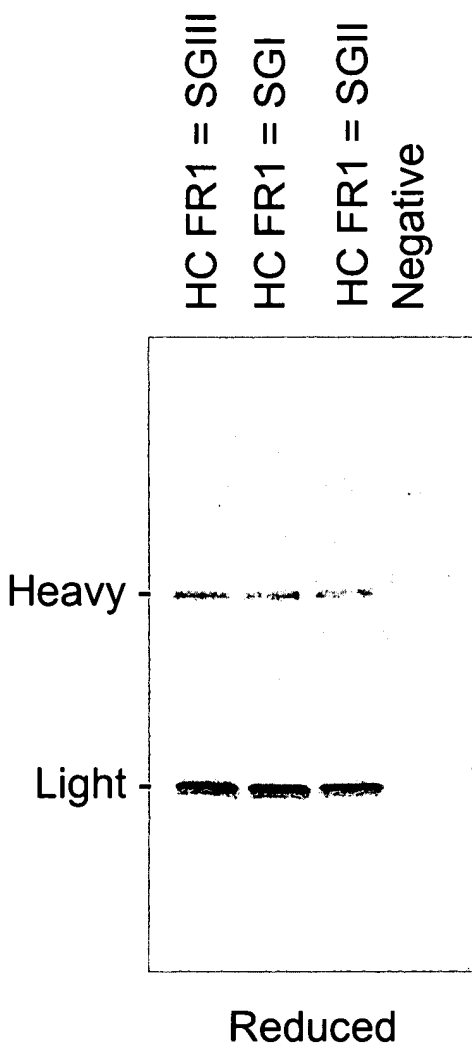
**Fig. 1B**



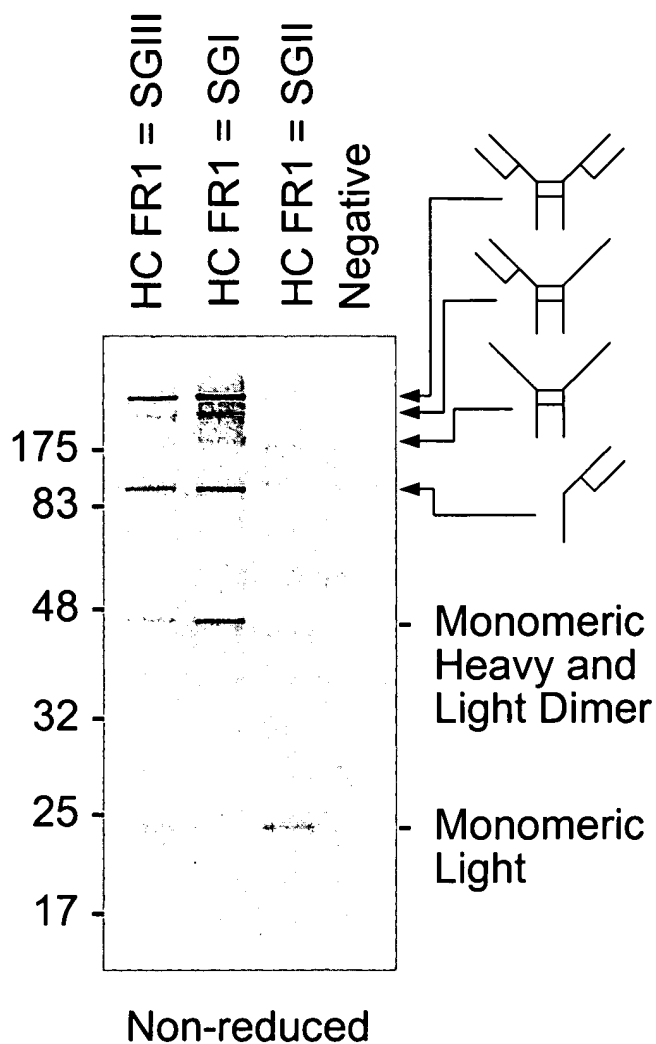
**Fig. 2**



**Fig. 3A**



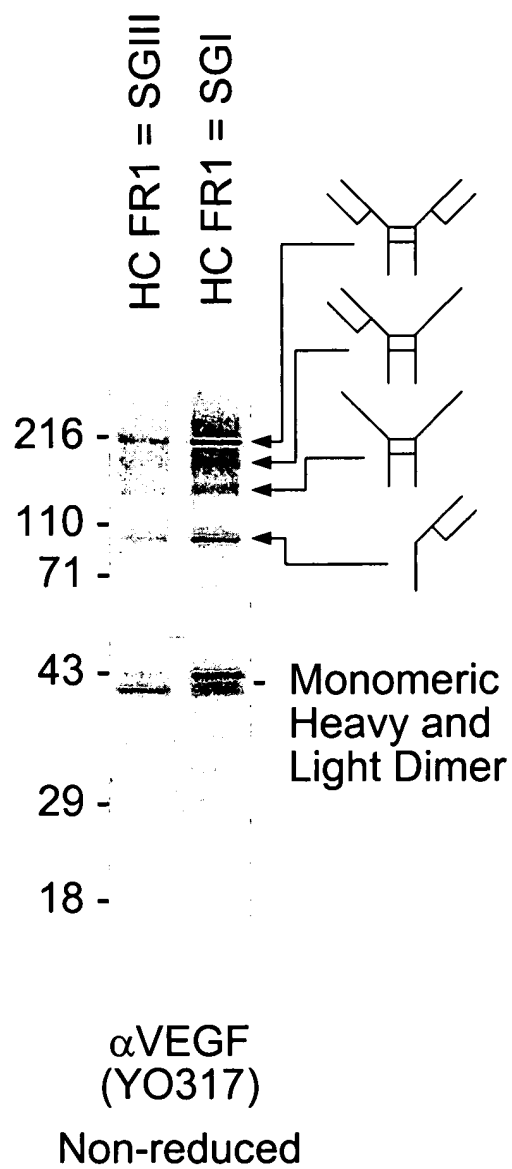
**Fig. 3B**



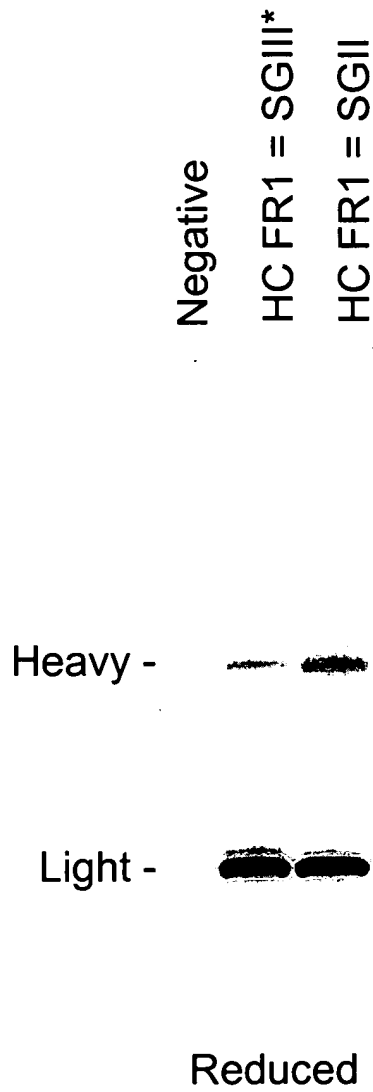
**Fig. 4A**



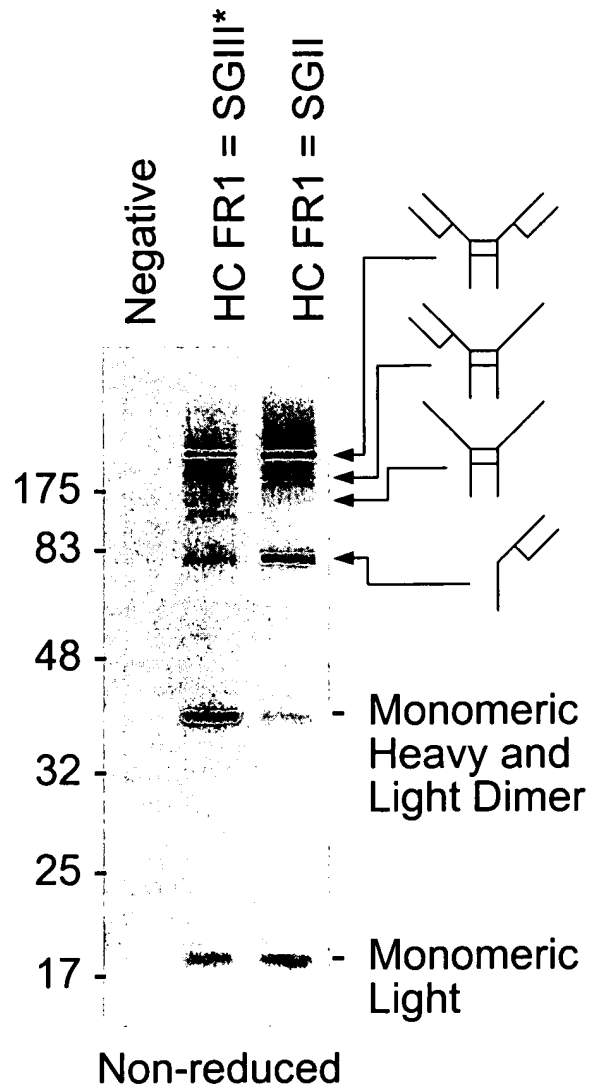
**Fig. 4B**



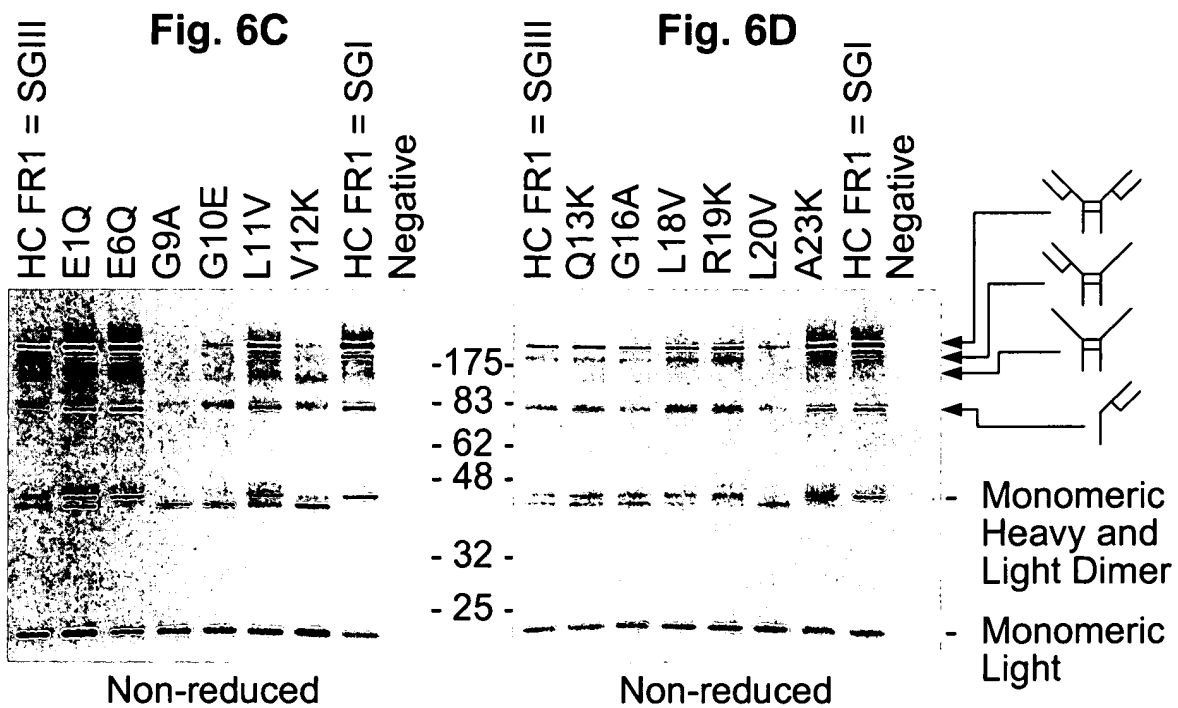
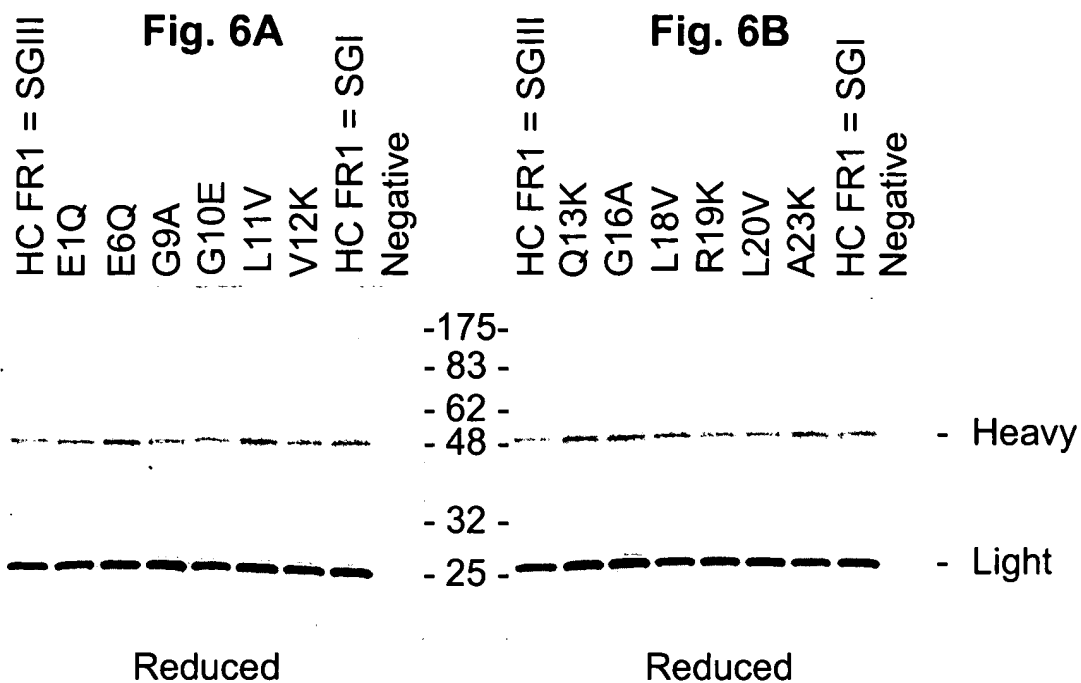
**Fig. 5A**



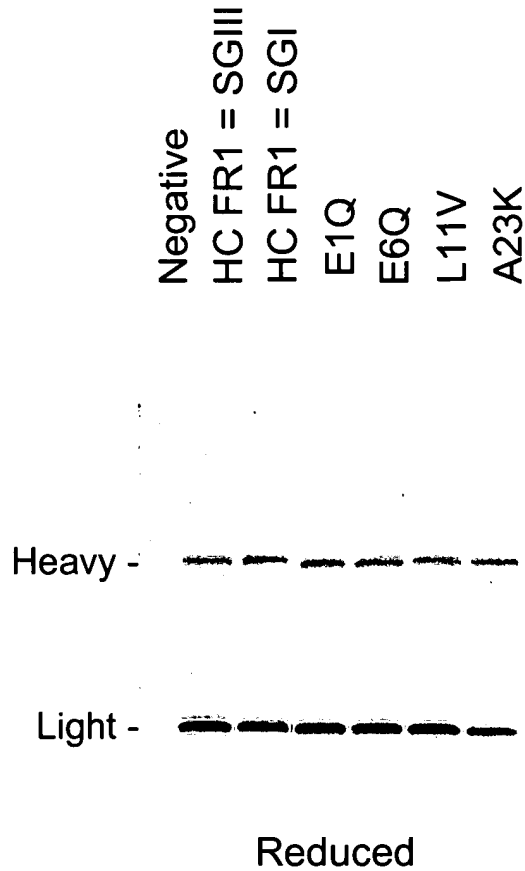
**Fig. 5B**



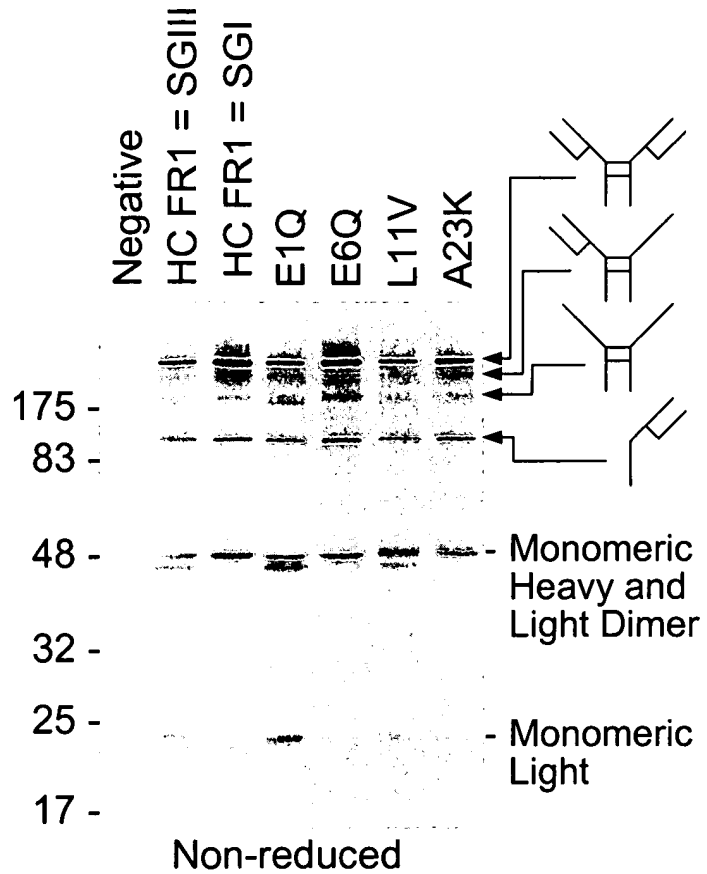
\*Includes an A24V change as part of humanization.



**Fig. 7A**

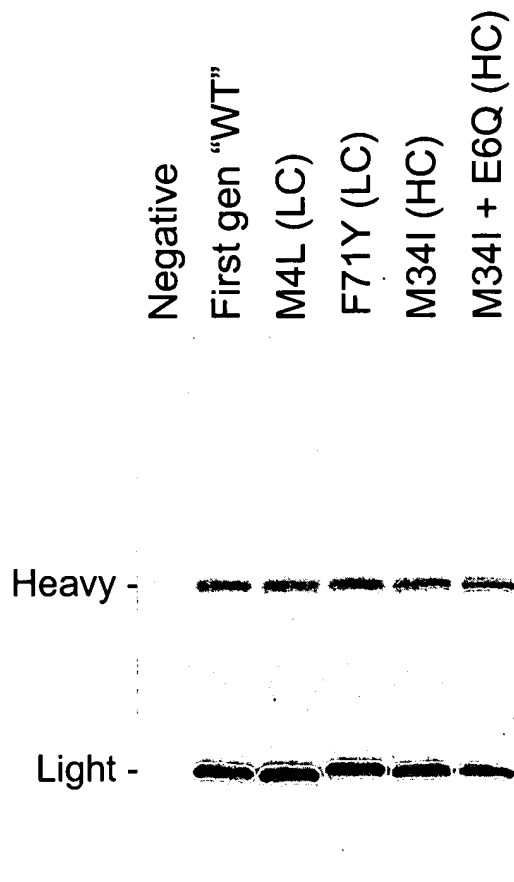


**Fig. 7B**

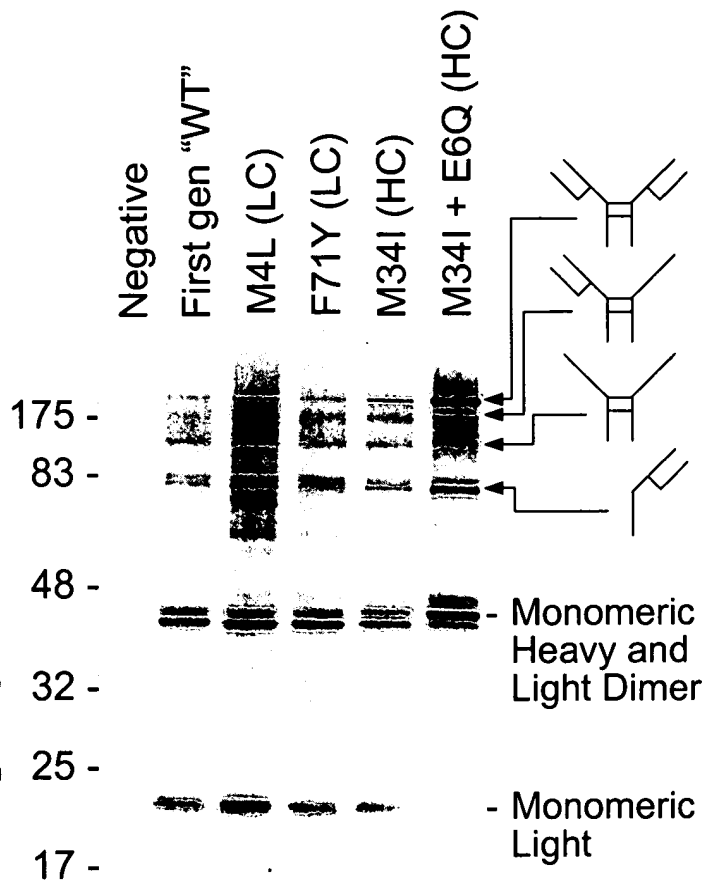




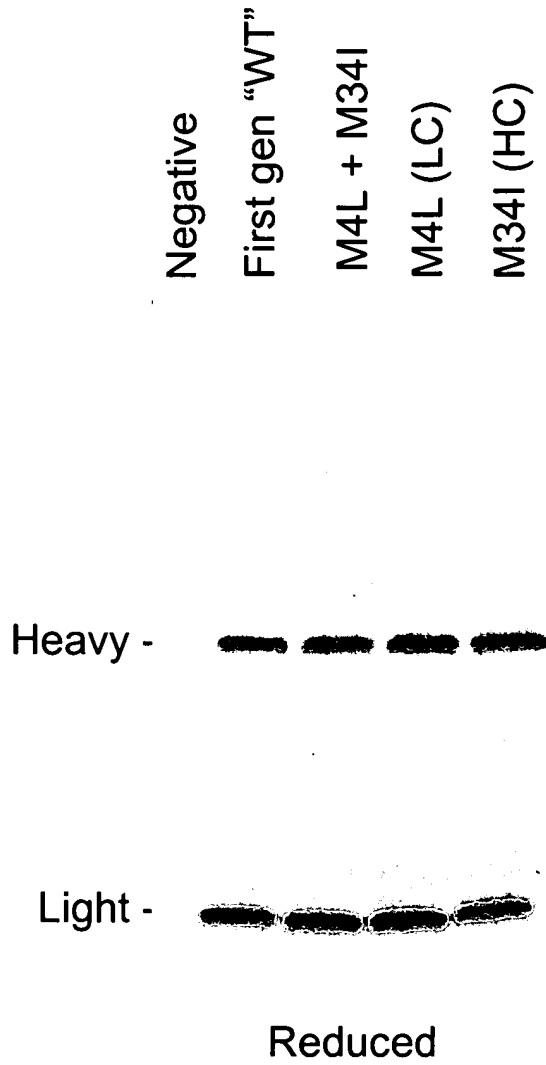
**Fig. 8A**



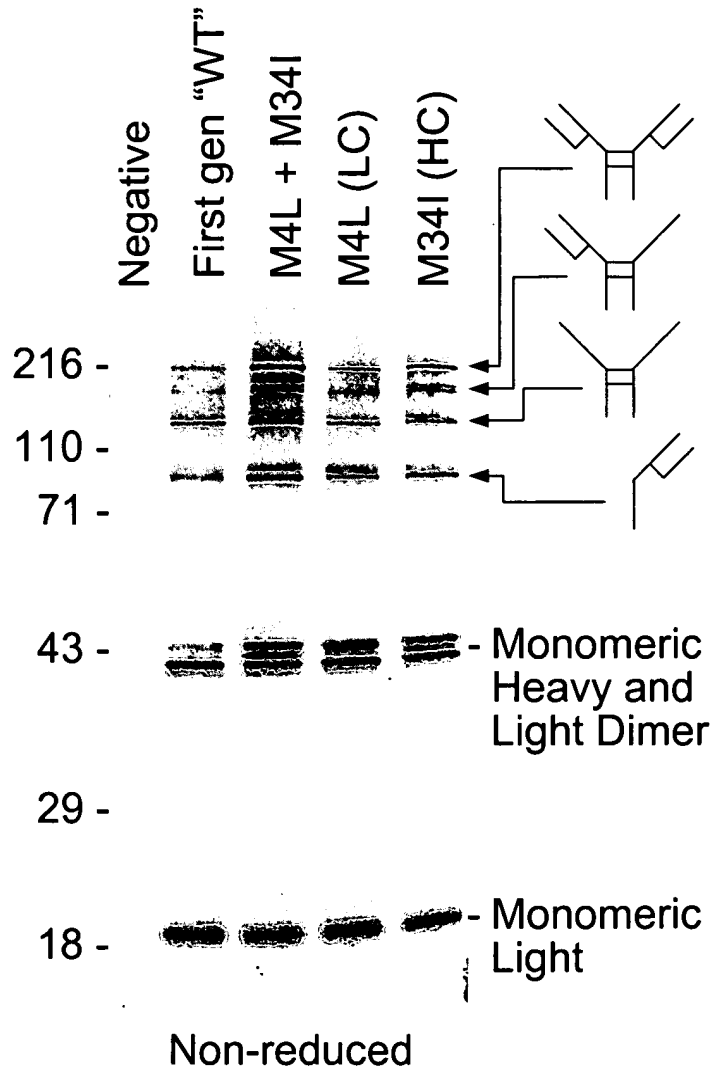
**Fig. 8B**



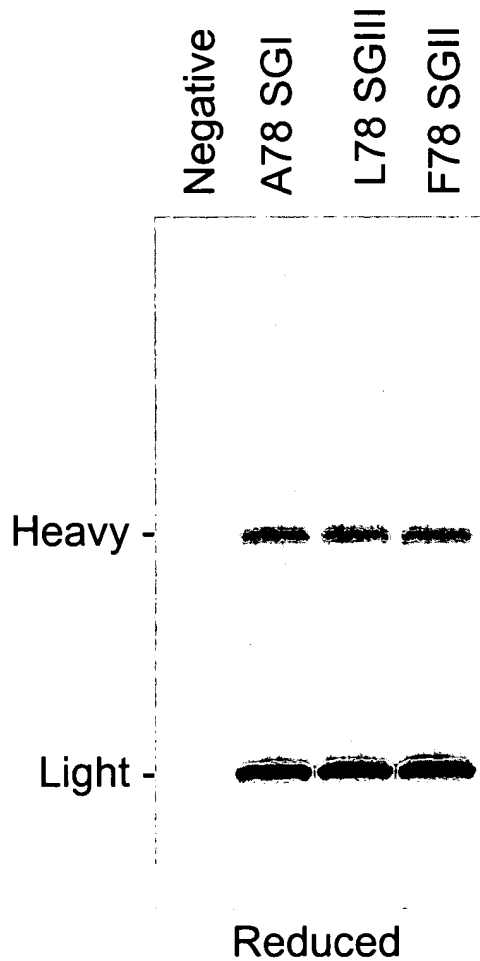
**Fig. 9A**



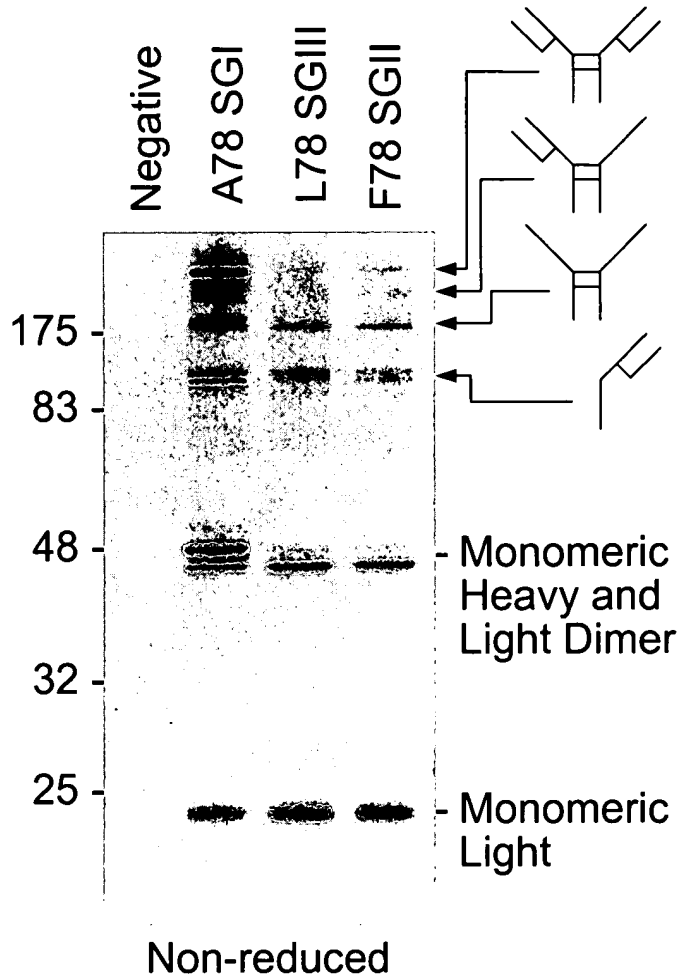
**Fig. 9B**



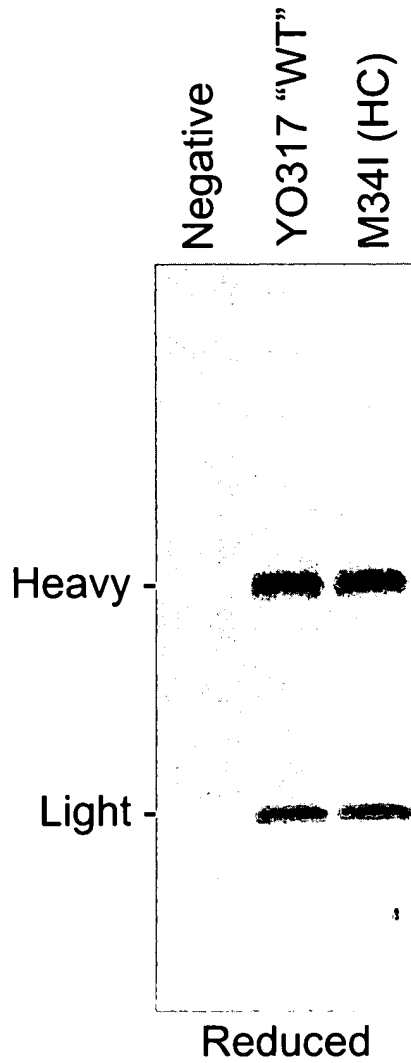
**Fig. 10A**



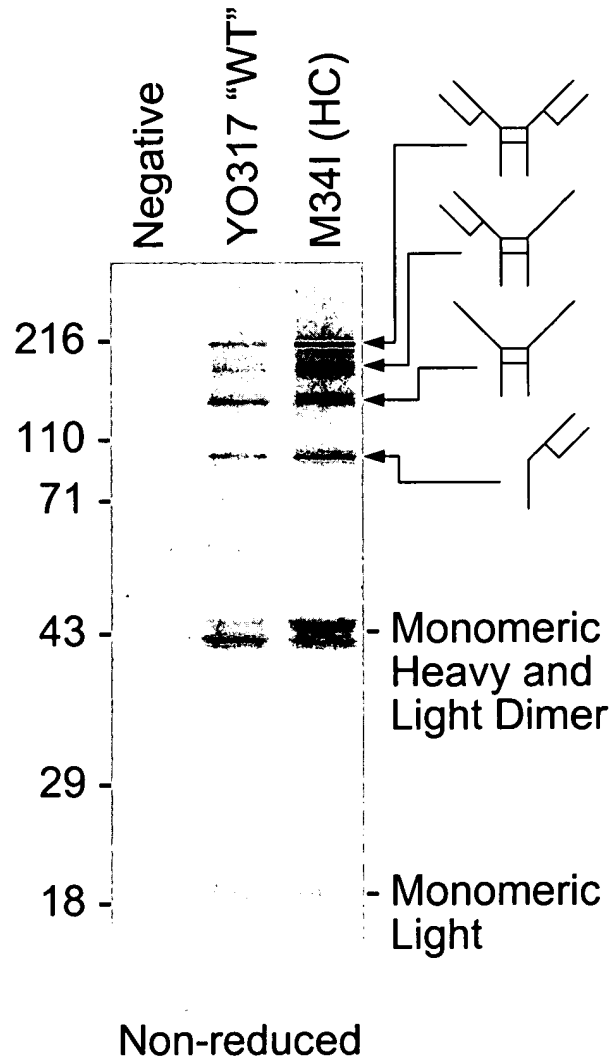
**Fig. 10B**



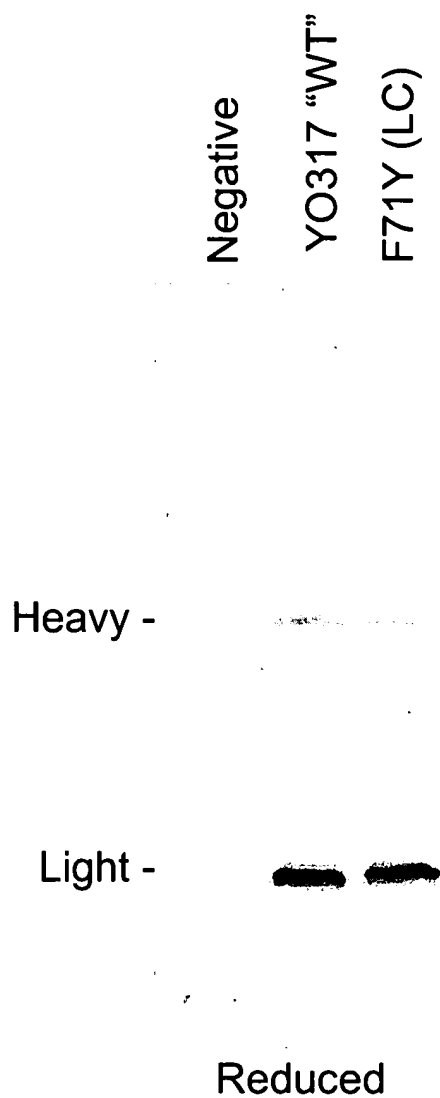
**Fig. 11A**



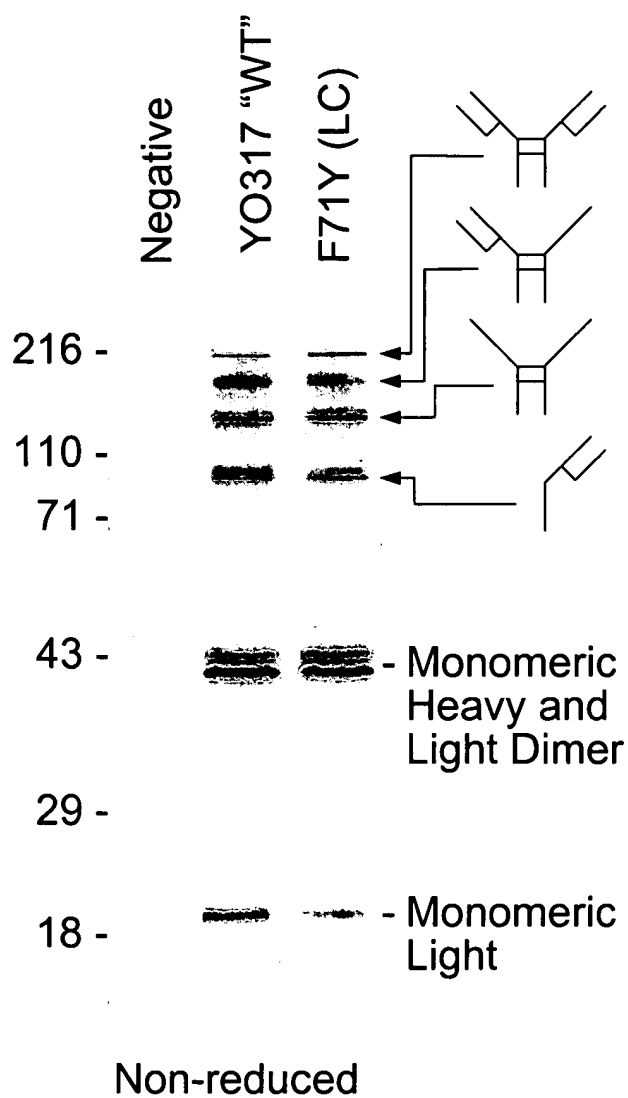
**Fig. 11B**



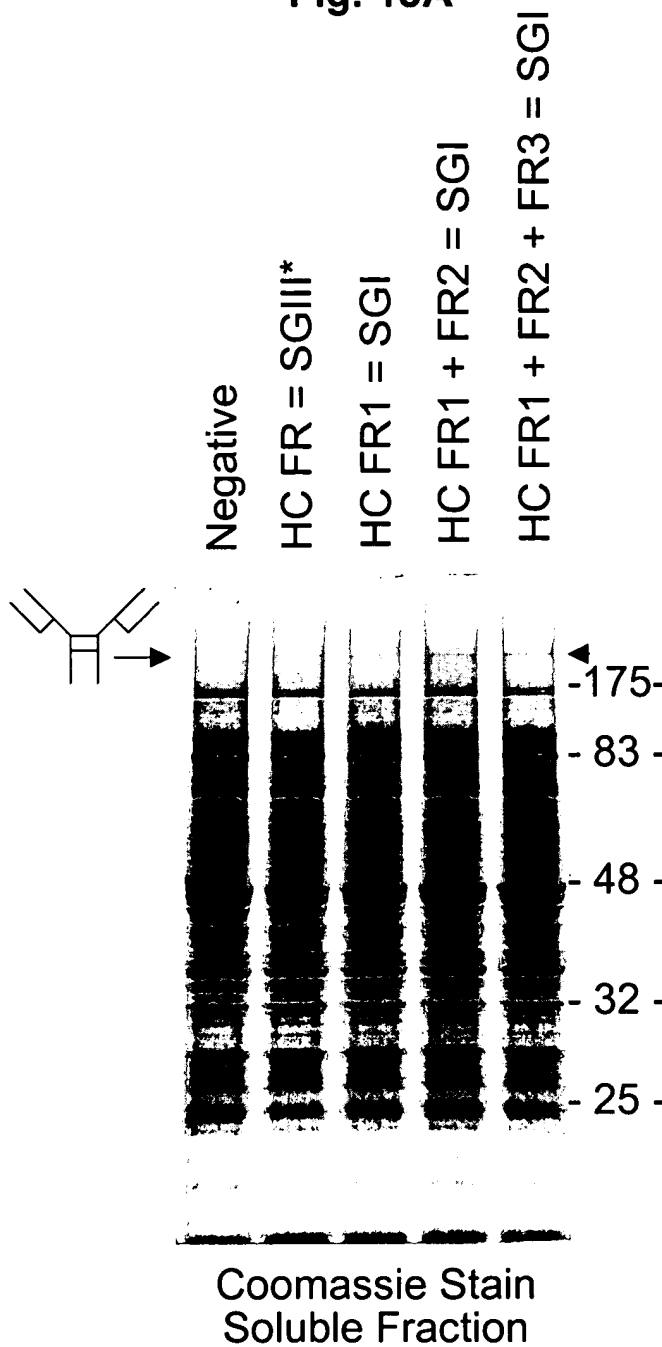
**Fig. 12A**



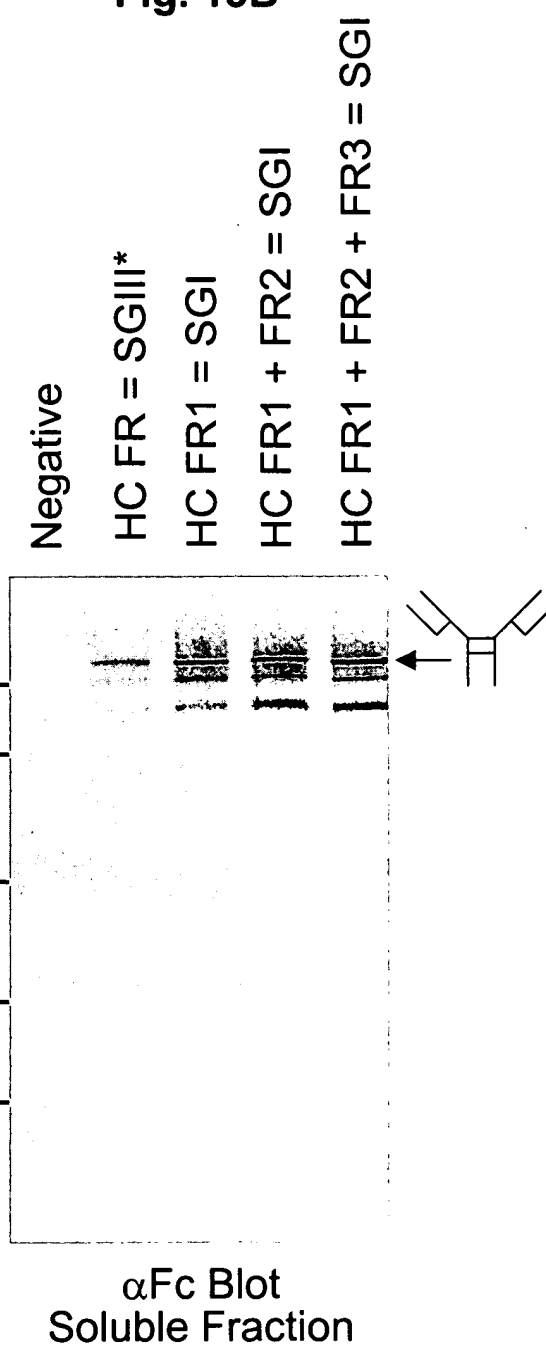
**Fig. 12B**



**Fig. 13A**



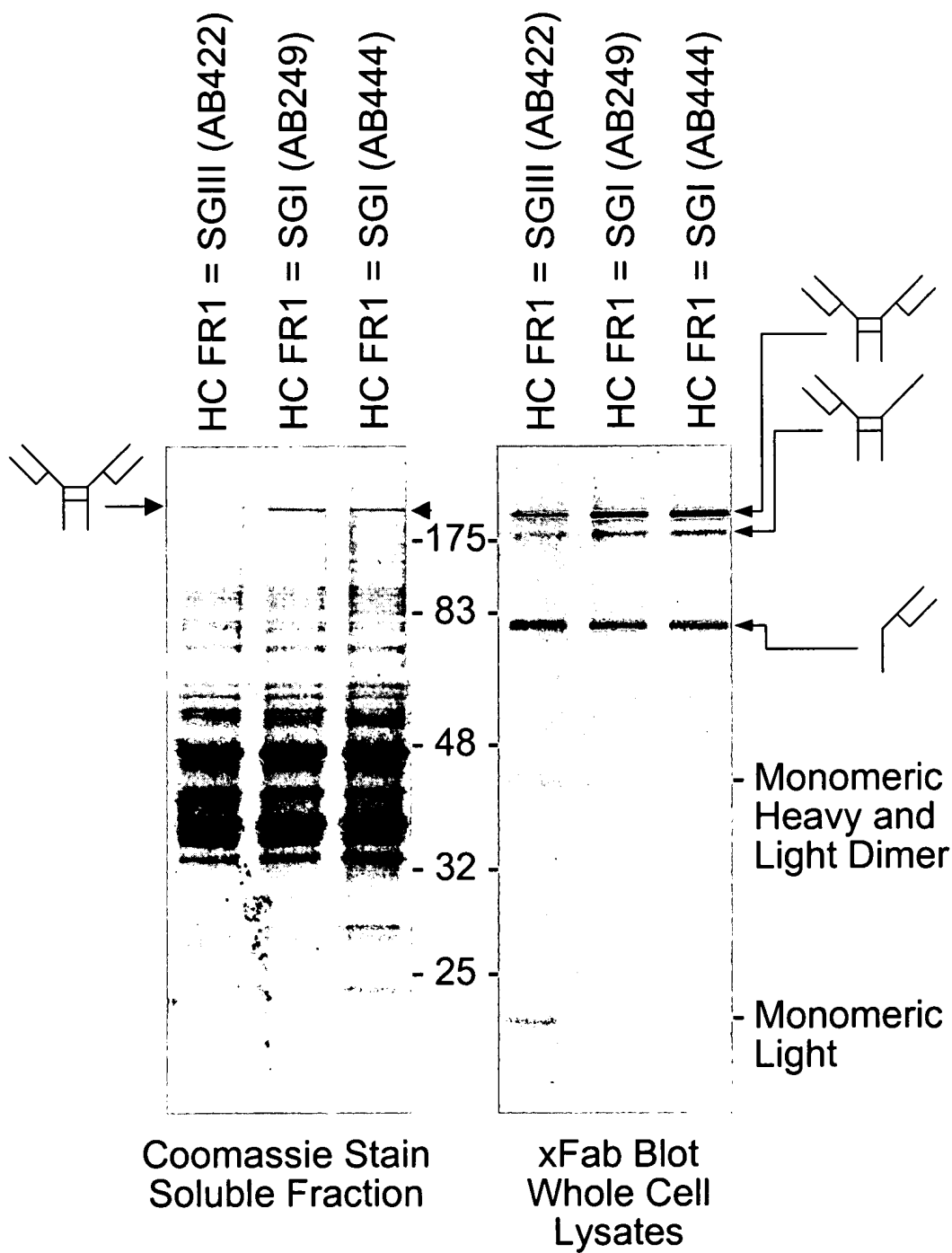
**Fig. 13B**



\* Except for residues changed during humanization.

**Fig. 14A**

**Fig. 14B**



# FIG. 15A

```

1  GAATTCAACT TCTCCATACT ITGGATAAGG AAATACAGAC ATGAAAAATC TCATTGTCTG GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
   CITTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTATG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATATG GGCCAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
   CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGGTTATAC CGGTTTTC TGGTTGTGCG CAACTAATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAAGTA
   CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACA GCTGTCTATA AGTGTCTACG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
   TTTTCAATTA GAAAAGTTGT CGACAGTATT TCACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTCCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGCTA CGCTGATATC
   AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTCGCGAT GCGACTATAG
   1      M K K N I A F L L A S M F V F S I A T N A Y A D I
           ^STII Signal TIR -1      anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGAG CTCCTGTTC GCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
   GTCNACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG AGCTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
   ^variable light (VL) cys

601 ATCAACAGAA ACCAGGAATA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC
   TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCGAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
   CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCAATATCG TGGCACGGCA CTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
   ^Variable light cys

801 AAGGTGGAGA TCAAAACGAAC TGTGGCTGCA CCACTGTGCT TCACTTTCCC GGCATCTGAT GAGCAGTTGA AATCTGGNAC TGCTTCTGTT GTGTGCCTGC
   TTCCACCTTT AGTTTGTCTG ACACCGAGT GGTAGACAGA AGTAGAAGGG CGGTACTACTA CTGCTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
   Constant Light cys^

```



## FIG. 15B

```
901 TGAATAACTT CTATCCCGA GAGGCCAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGTAACATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTAITGAA GATAGGCTCT CTCCGGTTTC ATGTACCTT CCACCTATTG CGGAGAGTTA GCCCAITGAG GGTCTCTTCA CAGTGCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
    1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC
    CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys
    1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCTCT ACGCCGAGC CATCGTGGC AGCTCGGTAC CGGGGATCT AGGCCTAACG
    AGCGGGCAGT GTTCTCGAA GTTGTCCTCT CTCACAATTA ATTTAGAGA TCGCGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCCTAGA TCCGGATTCG
226 S P V T K S F N R G E C O
    ^cys to bind heavy
    start lambda t0 terminator^
    1201 CTGGGTTGCC GCGGGGCGTT TTTTATGTT GCGAGCGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAAACG CGGCCCGCAA AAAATAACAA CGGCTGGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
    ^end lambda t0 terminator
    1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
    GCGTIATACC GCGTTTTACT GGTGTGCGC AACTAATCTAG TCCATCTCCC CCGCGACATG CTCCAITTCG GGTACGGTC GTAAAGGACTG CTGCTATGCC
    1401 AGCTGCTGG CGATTACGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTATATAA GTTGTACAGG CCGAGACTTA
    TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAG AGCAGTCAAT TTTCNAITTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
    1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAACCTAG TACGCAAGTT CACGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCAATAGATC TTAATACTTC TTCTTATAGC GTAAAGAGA
    M K K N I A F L L
    ^STII Signal TIR-1
    1601 TGCACTATG TTCGTTTTTT CTATTGCTAC AAACGGCTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCCTGTGTC AGCCAGGGGG CTCACCTCGT
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTGCGCATG CGACTCCAAG TCGACCACTT CAGACCGCCA CCGGACCAAG TCGGTCCCC GAGTGAGGCA
    10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
    ^anti-VEGF heavy chain (VNERK version)
    1701 TTGTCTCTGG CAGCTTCTGG CTATACCTTC ACCAACTAG GTATAAATG GGTCCGTGAC GCCCGGGTA AGGGCCTGGA ATGGGTTGGA TGGATTAAACA
    AACAGGACAC GTCGAAGACC GATATGGAAG TGCTTGATAC CATATTTGAC CCAGGCACTC CGGGGCCCAT TCCCGGACCT TACCCAACTT ACCTAATGT
    43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys
    1801 CCTATACCGG TGAACCGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
    GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAGTGA AAAAGAAATC TGGGAGGTT TTGCTGTGCT ATGACCGTCT ACTTGTGCGA
    77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
```

## FIG. 15C

1901 GCGCGCTGAG GACACTGCGG TCATTACTAG TGCAAAAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGTCTG GGGTCAAGGA  
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTCATG GCGGTGATTA TACACTTGCT CGCTTCTCG GTGACCATAA AGTGCAGAC CCCAGTTCTT  
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G  
^VH cys

2001 ACCCTGGTCA CCGTCTCCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCCTGGGCT  
TGGGACCAGT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAGAAGGG GGAACCGTGG AGGAGTTCT CGTGGAGACC CCCGTGTGCG CGGGACCCGA  
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C  
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGA CTACTTC CCGAACC CGGTGGTCT GTGGA ACTCA GCGGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCTCTC  
CGGACCAGTT CCTGATGAAG GGGCTTGGC ACTGCCACAG CACTTGAGT CCGCGGGACT GGTGCGCCGA CGTGTGGAAG GGCCGACAGG ATGTCAGGAG  
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

2201 AGGACTCTAC TCCCTCAGCA GCGTGGTGAC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCGC CAACACCAG  
TCCTGAGATG AGGAGTCTGT CGCACCACTG ACACGGGAGA TCGTCGAACC CGTGGGTCTG GATGTAGAG TTGCACCTTAG TGTTCGGGTC GTTGTGGTTC  
210 G L Y S L S V V T V P S S S L G T Q T Y I C N V N H K P S N T K  
^CH1 cys

2301 GTGACACA GA GTTGAGCC CAAATCTTGT GACAAAACTC ACACATGCC ACCGTGCCCA GCACCTGAAC TCCTGGGGG ACCGTCAATC TTCTCTTTCC  
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTGTAG TGTGTACGG TGGCAGGGT CGTGGACTTG AGGACCCCGC TGGCAGTCAG AAGGAGAAGG  
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P  
^cys to bind light chain ^hinge cys

2401 CCCCAAAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTGACA TGGTGTGGTG TGGACGTGAG CCAGGAAGAC CCTGAGGTCA AGTTCAACTG  
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCTTGGG ACTCCAGTGT ACGCACACC ACCTGCACCTC GGTGCTTCTG GGA CTCCAGT TCAAGTTGAC  
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W  
^Constant Heavy 2 (CH2) cys

2501 GTACTGTGAC GGCCTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCAGTAC CAGTGTGGTCA GCGTCTCTAC CGTCTGTGAC  
CATGACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GGGCCCTTCC TCGTCATGTT GTGCTGATG GCACACCACTG CGCAGGAGTG GCAGGACCTG  
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

2601 CAGGACTGGC TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAAG CCTCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA GGGCAGCCCC  
GTCTGTGACG ACTTACCGTT CCTCATGTT CCGTGTGTTG GGTGTTTCG GAGGGGTGG GTGTAGTCTCT TTTGGTAGAG GTTTCGGTTT CCGTCTGGGG  
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R  
^CH2 cys

2701 GAGAACCA CA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACCAAGTCA GCGTACCTG CCTGGTCAA GGGTCTCTATC CCAGCGACAT  
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTCTCAGT CGGACTGGAC GGACCACTTT CCGAAGATAG GGTCTGCTGA  
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I  
^Constant Heavy 3 (CH3) cys

## FIG. 15D

```
2801 CGCGTGGAG TGGGAGGCA ATGGGAGGC GGAGAACAAC TACAAGACA CGCTCCCGT GCTGGACTCC GAGGCTCCT TCTTCTCTA CAGCAAGCTC
    GCGCACCTC ACCTCTCGT TACCGTCCG CTTCTTGTTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGG AGAAGGAGAT GTCGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGACGAGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTGTTCCAC CGTCGTCCG TGCAGAGAAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGATGT CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CGCGCGGGCG TTTTATTG TTAACATG TTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCCAAC GCGCGCCCGC AAAAAATAAC AATTGAGTAC AAACGTGTCA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator
    ^start of tet resistance promoter ^start of tet resistance promoter
    ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGC ACCGTGTATG AAATCTAACA ATGCGTCTCAT CGTCATCCTC GGCACCGTCA
    TTGGAATTA CGCCATCAA TAGTGTCAAT TTAACGATTG CGTCAGTCGG TGGCACATAC TTAGATTGT TAGCGGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGGCCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCACGA
3301
```

## FIG. 16A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATT TTAGCTTGCCC AAAAAGAAGA AGAGTCGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGGTTATAC CCGGTTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGGGCTGTA CGAGGTAAAG CCGATGCGA GCATTCCTGA CGACGATAGG GAGCTGCTGC GCGATTAGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA  
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTGTCAAG GCGGAGCTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAAC TA GTACGCCAAGT  
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCAGGTAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC  
AGTGCAITTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
^STII Signal TIR -1 Anti-VEGF Light chain (version Y0317)^

501 CAGTTGACC AGTCCCGAG CTCCTGTGCG GCGATAGGTT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT  
GTCAACTGG TCAGGGGCTC GAGGACACAG CGGTATCCCA GTGCTAGTGG ACCTCGCGTT CAGTCTCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC  
TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AGAGCGAAG AGACCTAGGC CAAGACCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAATTTACT CTGACCATCA GCAGTCTGCA GCAGAAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGAGTTTGG ACAGGGTACC  
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGGTTGAA TAATGACAGT TGTCTATCG TGCACGCGCA CCTGCAAAAC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGCG  
TTCCACCTCT AGTTGTCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACAGAGACAA CACACGGAGG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAC GCCTCTCAAT CCGGTAATCT CCAGGAGAGT GTCACAGAGC AGCAGACAA  
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGTTA GCCCATTAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 16B

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGGCCTGAGC  
 CCTGTCGTGG ATGTCGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGACGCTTC AGTGGTAGT CCGGACTCG  
 193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
  
 1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCTCTT ACGCCGAGG CATCTGGGTAC CGGGGATCT AGSCCTAAGG  
 AGCGGCGAGT GTTCTCGAA GTTGTCCTTCT CTCACAAATTA ATTAGGAGA TCGCGCCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGAATTGC  
 226 S P V T K S F N R G E C O  
  
 1201 CTCGGTTGCC GCGGGCGGTT TTTTATTGTT GCGGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCCAC TGCAATGCTT  
 GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACCTTACGAA  
  
 1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG  
 GCCTTATACC GCCTTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCATTTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC  
  
 1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTCACACAG CTGTCATAAA GTTGTCAOCC CCGAGACTTA  
 TCGACGACGC GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAAITTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT  
  
 1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TAGCCTAAGT CAGCTAAATA GGTATCTTAG AATTATGAG AAGAATATCG CATTTCTTCT  
 ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA  
 1 M K K N I A F L L  
 ^StII Signal TIR-1  
  
 1601 TGCACTATG TTCTTTTCTT CTATTGCTAC AAACGCGTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCTGGTGC AGCCAGGGGG CTCACCTCGT  
 ACCTAGATAC AAGCAAAAAA GATAACGATG TTTCGCGCATG CGACTCCAAG TCAGCCACCT CAGACCGCCA CCGGACCAGG TCGGTCCCC GAGTGAGGCA  
 10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
 ^Anti-VEGF Heavy Chain (version Y0317)  
  
 1701 TTGTCCTGTG CAGCTCTG CAGCTCTG CTACGACTTC ACACGACTAG GTATGAATG GTCTCGTAC GCGCCGGTGA AGGCGCTGGA ATGGGTTGGA TGGATTAAACA  
 AACAGGACAC GTCGAAGACC GATGCTGAAG TGGTGTGATG CATACTGAC CCAGGCGCAT CCGGGCCCAT TCCCGGACCT TACCNAACCT ACCTAATGT  
 43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T  
  
 1801 CCTATACCG TGAACCGACC TATGCTGCGG ATTTCAAACG TCGTTTCACT TTTTCTTTAG ACACCTCCA AAGCACAGCA TACCTGCAGA TGAACAGCCT  
 GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTC AGCAAGTGA AAAAGAAATC TGTGGAGTT TGTGTGCTT ATGACGCTT ACTTGTGCGA  
 77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L  
  
 1901 GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAAGTAC CCGTACTATT ATGSGACGAG CCACTGGTAT TTGACGCTT GGGTCAAG AACCTTGGTC  
 CCGCGGACTC CTGTGACGCG AGATAATGAC ACCTTTCATG GGCATGATAA TACCTGTCTC GGTGACCAATA AAGTGCAGA CCCAGTTCC TTGGGACCAG  
 110 R A E D T A V Y Y C A K Y P Y Y G T S H W Y F D V W G Q G T L V  
  
 2001 ACCGTCTCTT CCGCCTCCAC CAAGGGCCCA TCGTCTTCC CCCTGGCACC CTCTCCAG AGCACTCTG GGGCACAGC GGCCTTGGC TGCTTGTCA  
 TGGCAGAGGA GCGGAGGTG GTTCCCGGT AGCCAGAAG GGGACCTGG GAGGAGTTTC TCGTGGAGAC CCCGTGTG CCGGAGCCCG ACGGACCACT  
 143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

## FIG. 16C

2101 AGGACTACTT CCCGAACCG GTACGGTGT CGTGGAACTC AGGCGCCCTG ACCAGCGCG TGCAACACCTT CCGGCTCTC CTACAGTCTT CAGGACTCTA  
TCTCTATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG GCACCTGGAC TGGTGGCGG ACCTGTGGAA GGGCCGACAG GATGTGAGG GTCTTGAGT  
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y  
2201 CTCCTCAGC AGCGTGGTA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAACTGTAAT CAAACACCAA GGAAGCAAG  
GAGGAGTGG TCGCACTACT GACACGGGAG ATCGTCGAAC CCGTGGTCTT GGATGTAGAC GTTGCACTTA GTTGTGGGT CGTGTGGT CCACCTGTTC  
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K  
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACCGTGCC AGCACCTGAA CTCCTGGGG GACCGTCACT CTCCTCTTC CCCCCAAAC  
TTTCAACTCG GGTTTAGAAC ACTGTTTGA GTGTGTACGG GTGGCACGGG TCGTGGACTT GAGGACCCCG CTGGCAGTCA GAGGAGAAG GGGGTTTTG  
243 K V E P K S C D K T H T C P P A P E L L G G P S V F L F P P K P  
2401 CCAAGACAC CCTCATGATC TCCCGACCC CTGAGGTAC ATGCGTGGT GTGGAAGTGA GCCAGAAGA CCTGAGGTC AAGTTCACT GGTACGTGA  
GGTTCCTGTG GGAGTACTAG AGGSCCTGG GACTCCAGTG TAAGCACAC CACTGCACT CGTGTCTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT  
277 K D T L M I S R T P E V T C V V P R E Q Y N S T Y R V V S V L T V L H Q D W  
2501 CGCGTGGAG GTGCATATG CCAAGACAA GCCGCGGGAG GAGCAGTACA ACAGCAGTA CGTGTGGTC AGCTCTCTCA CGTCTCTGCA CAGGACTGG  
GCCGACCTC CAGGTATTAC GGTTCCTGTT CGGCGCCCTC CTGCTCATGT TGTGTGCAT GGCACACGAG TCGCAGGAGT GGCAGGAGT GGTCTGACC  
310 G V E V H N A K T K P R E Q Y N S T Y R V V S V L T V L H Q D W  
2601 CTGAATGGCA AGGAGTACAA GTGCAAGTTC TCCAAACAA CCGTCCAGC CCCCATCGAG AAAACCATCT CCAAGCCAA AGGCGAGCC CGAGAACCAC  
GACTTACCGT TCCTCATGTT CAGGTTCCAG AGGTTGTTTC GGGAGGCTG GGGTAGCTC TTTGTGAGA GGTTCGGTT TCCGTCGGG CTCTTTGGT  
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q  
2701 AGGTGTACAC CCTGCCCCCA TCCCGGAAG AGATGACAA GAACAGGTC AGCTGACCT GCCTGTCAA AGGCTTCTAT CCCAGCACA TCGCGGTGA  
TCCACATGTG GGCAGGGGT AGGCCCTTC TCTACTGTT CTGTGTCAG TCGGACTGGA CGGACCACTT TCCGAAGATA GGTGCGCTGT AGCGCACCT  
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E  
2801 GTGGGAGC AATGGCAGC CGGAGAACA CTACAGACC AGCCTCCCG TCGTGGACT CGAGGCTCC TTCTCTCT ACAGCAAGT CACCGTGGAC  
CACCTCTCG TTACCGTGG GCCTCTTGT GATGTTCTG TCGGAGGCG ACGACCTGAG GCTGCCGAG AGAAGGAGA TGTCTTGA GTGGCACCTG  
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D  
2901 AAGAGCAGT GGCACAGGG GAAGTCTTC TCATGCTCG TGAATCATGA GGCTCTGAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA  
TTCTCTCCA CGTCTGTC CTTGCAGAAG AGTACGAGC ACTACGTACT CCGAGAGTGT TTGGTCACT GGTCTCTCT GAGAGGAG AGAGGCCAT  
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K  
3001 AATAAGCAT CGAGGCCCT AGATCCCTA AGCTCGGT GCGCGGGG GTTTTTTAT GTTAATCAT GTTTGACAGC TTATCATGA TAAGCTTAA  
TTATCTGTAC GCTGCCGGA TCTCAGGAT TCGAGGCCAA CGGCGCGCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGT ATTCGAAAT  
477 O  
3101 TGGGTAGT TATCAGTT AATTGTCTAA CGCAGTCAG CACCGTGT GAAATCTAAC AATGCGCTCA TCGTCATCT CGGCACGTC ACCCTGGAT  
ACCCATCAA ATAGTGTCAA TTTAACGAT GGTGAGTCC GTGGCACATA CTTTAGATT TTAGCGAGT AGCAGTAGA GCCGTGGAG TGGGACCTAC  
\*Start Tet Resistance Coding Sequence

## FIG. 16D

3201 CTGTAGGCAAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCTT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAC TATGGCGTGC TGCTAGCGCT  
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTTCGTA GCGGTCAGTG ATACCGCAGG ACGATCGCGA

3301

## FIG. 17A

```
1 GAATTCAACT TCCTCATACT ITGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCC AAAAAGAGA AGAGTCGAAT
  CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCTTCTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
  CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTGCG CAACTAACATA GTCCATCTCC

201 GGGGCGCTGA CGAGGTAAG CCGATGCCA GCATTCTTGA CGACGATAGG GAGCTGTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
  CCCGGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAGG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
  TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGNA TATCAGCGNA ACAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA

401 TCACGTAAAG AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGTGTATATC
  AGTGCATTTT TCCCATAGAT CTTAATACIT CTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
  1 M K K N I A F L L A S M F V F S I A T N A Y A D I
    ^Still Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCC GCCTGTGG GCGATAGGTT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
  GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTGACCA
  26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
    ^variable light (VL) cys

601 ATCAACAGAA ACCAGGAATA GCTCCGAAG TACTGAITTA CTTCACTCC TCCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAC
  TAGTTGCTTT TGGTCCTTTT CGAGGCTTTT ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTTG
  60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
  CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CTGCAAAACC TGTCCCATGG
  93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
    ^Variable light cys

801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
  TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG
  126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
    Constant Light cys^
```



## FIG. 17B

```
901 TGAATAAATT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGGATAAC GCCTCCAAT CGGTAATC CCAGGAGAGT GTACACAGAG AGGACAGCAA
ACTTATTGAA GATAGGTTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CCGAGAGTTA GCCCATAGAG GGTCTCTTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGCCTGAGC
CCTGTCTGTG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CCGACGCTTC AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGAGC CATCGTGGCG AGTCGGTAC CCGGGATCT AGGCCTAAGC
AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGGAGA TCGGCGCTGC GTAGCACGC TCGAGCCATG GSCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
^cys to bind heavy start lambda t0 terminator^
1201 CTGGTTGCC GCGGGGGTT TTTTATTGTT GCGGCGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCAAACG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda t0 terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGAATTGATC AGGTAGAGGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
CGTTATATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTGCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGTGTCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATPCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCTAFAA GTTGTACGG CGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCAATTAG AAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTCTGAAT
1501 TAGTGTCTTT GTTTTATTT TTAAATGAT TTGTAACCTAG TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAATAAA AAATTACATA AACATTGATC ATCGGTTCAA GTGCATTTT CCCATAGATC TTAATATCTT TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTGGTTTTTT CTATTGCTAC AAACGGCTAC GCTCAGGTTT AGCTGGTGCA GTCTGCGCA GAGGTGAAAA AGCCAGGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAA GATAACGATG TTTCGCGATG CGAGTCCAGT TCGACCCAGT CAGACCGCGT CTCCACTTTT TCGGTCCCGG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
^anti-VEGF Heavy Chain (VNERK version)
^Heavy Chain FR1 changed to SubgroupI consensus sequence
1701 GTATCTGTA AAGCTTCTGG CTATACCTTC ACCAATATG GTATAAATG GGTCCGTGAG GCGCCGGTA AGGCGCTGGA ATGGTTGGA TGGATTAAACA
CATAGACAT TTCGAAGACC GATATGGAAG TGTTTGATAC CATATTTGAC CCAGGCGATC CCGGCGCCAT TCCCGACCT TACCCACCT ACCTAATGT
43 V S C K A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys
1801 CCTATACCG TGAACGACC TATGCTGGG ATTTCAACG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCAGACA TACCTGCAGA TGAACAGCCT
GGATATGCC ACTTGCTGG ATACGAGCC TAAAGTTGCG AGCAAGTGA AAAAGAAATC TGTGAGGTT TTCGTGTCTG ATGGACGCT ACTTGTCCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
```

# FIG. 17C

1901 GCGGCTGAG GACACTGCG TCTATTACTG TGCAAGTAC CGCAGTATT ATGTGAACGA GCGGAAGAGC CACTGTGATT TCGACGTCTG GGTCAAGGA  
CGCGGACTC CTGTGACGGC AGATAATGAC AGTTTTCATG GCGTGATAA TACATTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCTT  
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G  
^VH cys

2001 ACCCTGGTCA CGCTCTCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CTGGGACCC TCCTCCAAGA GCACCTCTTG GGGCACAGCG GCCCTGGGCT  
TGGGACCAAT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAGAAGGG GGACCGTGGG AGGAGTTCT CGTGGAGACC CCCGTGTGCG CGGGACCCGA  
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C  
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTC CCGAACC GGCGCTGTC GTGGAATCA GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCT TACAGTCTTC  
CGGACCAAGT CTGATGAAG GGCCTTGGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GTGCGCGCA CGTGTGAAG GGCCGACAGG ATGTCAAGAG  
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S  
^CH1 cys

2201 AGGACTCTAC TCCTCTAGCA GGTGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG  
TCCTGAGATG AGGAGTCTG CGCACCACTG ACACGGGAGA TGTGCGAACC CTTGGGTCTG GATGTAGACG TTGCACITTAG TGTTCGGGTC GTTGTGTTTC  
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K  
^CH1 cys

2301 GTGACAAGA AAGTTGAGCC CAAATCTTGT GACAAAATC ACACATGCC ACCTTGCCCA GCACCTGAAC TCCTGGGGG ACCGTCTAGTC TTCCTCTTCC  
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTTGAG TGTGTACGG TGGCACGGGT CGTGGACTTG AGGACCCCCC TGGCAGTCAG AAGGAGAAGG  
243 V D K K V E P K S C D K T H T C P P A P E L L G G P S V F L F P  
^cys to bind light chain ^hinge cys

2401 CCCCAAAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTACA TGGTGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCACATG  
GGGTTTTTGG GTTCTGTGG GAGTACTAGA GGGCCTGGG ACTCCAGTGT ACGCACACC ACCTGCACCT GGTGCTTCTG GGAATCCAGT TCAAGTTGAC  
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W  
^Constant Heavy 2 (CH2) cys

2501 GTAGTGGAC GGCCTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACA CAGCACGTAC CGTGTGTGTC GGTCTCTAC CGTCTCTGAC  
CATGACCTG CCGACCTCC ACGTATTACG GTTCTGTTC GCGGCCCTCC TCGTCATGTT TCGTGTGATG GCACACCATG CGCAGGAGTG GCAGGACGTG  
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

2601 CAGGACTGGC TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAGC CTCTCCAGC CCCATCGAGA AAACATCTC CAAAGCCAAA GGGCAGCCCC  
GTCTGACCG ACTTACCGTT CCTCATGTT CCGTCCAGA GGTGTGTTG GAGGGGTGG GGTGAGTCT TTTGGTAGAG GTTTCGGTTT CCCGTCCGGG  
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R  
^CH2 cys

2701 GAGAACCAAC GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACCAAGTCA GCTTGACTG CCTGGTCAA GGTCTCTATC CCAGCGACAT  
CTCTTGGTGT CCACATGAG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTTCCAGT CGGACTGAC GGAACAGTTT CCGAAGATAG GGTCTGCTGA  
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I  
^Constant Heavy 3 (CH3) cys

## FIG. 17D

```
2801 CGCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTA CAGCAAGCTC
    GCGCACCTTC ACCCTCTCGT TACCCGTGGG CCTCTTGTTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTCCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AAGCTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAGA GACGAGGCA CTACGTACTC CGAGACGCTG TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGGTAA ATAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCCGGGCG TTTTATTG TTAAGTATG TTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCGTACG CTGCCGGAT CTCAGGGATT GCGAGCCCAAC GCGGCCCGC AAAAAATAAC AATTGAGTAC AAAGTGTGCA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator ^start of tet resistance promoter
    ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACGTGATATG AAATCTAACA ATGCGCTCAT CGTCATCCTC GGCACCGTCA
    TTGGAATTA CGCCATCAA TAGTGTCAT TTAACGATTG CGTCAGTCCG TGGCACATAC TTAGATTGT TAGCGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTCTC
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AAGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCACTGA TACCGCACGA
3301
```

## FIG. 18A

```
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
  CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCGT TACTTTTITAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAAGTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACACAGG GTTGATTGAT CAGGTAGAGG
  CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGCGTTATAC CGCGTTTITAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGGATGCCA GCATTCTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
  CCGCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GGTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACAA GCTGTCTATAA AGTTGTACAG GCGGAGACTT ATAGTCGCTT TGTTTTITAT TTTTAATGTA TTTGTAACCTA GTACGCCAAGT
  TTTTCAATTA GAAAAGTTGT CGACAGTAAT TCACAGTGTC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCAGGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTCTCTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
  AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGTAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
  1 M K K N I A F L L A S M F V F S I A T N A Y A D I
    ^STII Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCCGAG CTCCTGTGCC GCGTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TPAAACTGGT
  GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGGTATCCCA GTGGTAGTGG AGCTGCGGTT CAGTCCCTATA ATCGTTGATA AATTGACCA
  26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
    ^variable light (VL) cys

601 ATCAACAGAA ACCAGGAATA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC
  TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTTG
  60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCAGAAAGAC TTGCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTGG ACAGGGTACC
  CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCTATATCG TGGCACGCGCA CCTGCAAAACC TGTCCCATGG
  93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
    ^Variable light cys

801 AAGGTGGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
  TTCACCTCTT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG AGAAGACAA CACACGGAGC
  126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
    Constant Light cys^
```

# FIG. 18B

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901 TGAATAACTT CTATCCAGA GAGGCAAG TACAGTGAA GTGGATAAC GGCCTCCAAT CGGTTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTAITGAA GATAGGGTCT CTCCGGTTTC ATGTACACTT ACACCTATTG CGGGAGGTTA GGCCTCTTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC
    CCTGTCTGG AGTCTGGAGT CGTCGTGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCCTCT ACSCCGGAG CATCTGGTAC CCGGGGATCT AGGCCTAACG
    AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTTAGAGA TCGGGCCCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O ^cys to bind heavy
    start lambda t0 terminator^
1201 CTCGGTTGCC GCGGGCGT TTTTATTCTT GCGAGCGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAACGG CGGCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
    ^end lambda t0 terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGTAGAGGG GGGGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
    CGGTATATACC GCGTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCCC CCGGACATG CTCCATTTCG GGTACGGTC GTAAAGGACTG CTGCTATGCC
1401 AGTGTCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TGCTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACGG CCGAGACTTA
    TCGAGGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCATTAAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TAGGCAAGTT CAGTAAAAA GGTATCTTAG AATTATGAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCGATAGATC TTAATACTTC TTCTTATAGC GTAAAGAGA
    M K K N I A F L L
    ^STII Signal TIR-1
1601 TGCACTATG TTCGTTTTTT CTATGCTAC AAAGCGTAC GCTCAGGTTC AGCTGCAAGA GTCTGGCCCG GGCCTGGTGA AACCATCTCA GACTCTCTCC
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGAGTCCAAG TCAGAGTTCT CAGACCGGCG CCGGACCATT TTGGTAGAGT CTGAGAGAGG
10 A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S Q T L S
    ^anti-VEGF heavy chain (VNERK version)
    ^Heavy chain FRI changed to Subgroup II consensus sequence
1701 TTGACTTGTA CTGTTTCTGG CTATACCTTC ACCAACTATG GTATAAATG GTTCCTGTCAG GCGCCGGGTA AGGCGCTGGA ATGGGTTGGA TGGATTAAACA
    AACTGAACAT GACAAAGACC GATATGGAAG TGGTGTGATAC CATATTGAC CCAAGGCAGTC CCGGGCCCAT TCCGGGACCT TACCCAACT ACCTAATGT
43 L T C T V S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys
1801 CCTATACCGG TGAACCGACC TATGTCGGG ATTTCAAACG TCGTTTCACT TTTTCTTTAG ACACCTCCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
    GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAAGTA AAAAGAAATC TGTGGAGGT TTGCTGTCTG ATGACAGTCT ACTTGTCCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

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## FIG. 18C

1901 GCGGCTGAG GACACTGCG TCTATTACTG TGCATAATGAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGTGTATT TCGACGTCTG GGGTCAAGGA  
CGCGGACTC CTGTGACGC AGATAATGAC AGTTTTCATG GGGGTGATAA TACACTTGCT CGCCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCTT  
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G  
^VH cys

2001 ACCTTGGTCA CGTCTCCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTTG GGGCACAGCG GCCCTGGCT  
TGGGACCACT GGCAGAGGAG CCGGAGGTGG TTCCCGGTA GCCAGAAGG GACCGTGGG AGGAGTTCT CGTGAGACC CCCGTGTGCG CGGGACCCGA  
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C  
Constant Heavy 1 (CH1) cys

2101 GCCTGGTCAA GGACTACTTC CCGAACC GG TACGGTGTG GTGGAATCA GCGGCCCTGA CCAGCGGCGT GCACACTTC CCGGTCTGCC TACAGTCTTC  
CGGACCACTT CTGATGAAG GGCCTTGCC ACTGCCACAG CACTTTGAGT CCGCGGACT GTCGCCGA CGTGTGAAG GCGCGACAGG ATGTCAGGAG  
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S  
^CH1 cys

2201 AGGACTCTAC TCCTCAGCA GGTGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG  
TCTGTAGATG AGGGAGTGT CGCACCACTG ACACGGGAGA TCGTCGAACC CGTGGTCTG GATGTAGACG TTGCACCTAG TGTTCGGGTC GTTGTGGTTC  
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K  
^CH1 cys

2301 GTGACACAAGA AAGTTGAGCC CAAATCTGT GACAAAATC ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTCAATC TTCCTCTTC  
CACTGTCTT TTCAACTCGG GTTTAGAAC CTGTTTGTAG TGTGTAGCG TGGCACGGGT CGTGACTTG AGGACCCCC TGGCAGTCAG AAGGAGAGG  
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P  
^cys to bind light chain ^hinge cys

2401 CCCCCAACCAAGGACACCT CTCATGATCT CCGGACCCC TGAGGTACA TCGTGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG  
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCCTGGG ACTCCAGTGT ACGCACACC ACCTGCACTC GGTGCTTCTG GACTCCAGT TCAAGTTGAC  
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W  
^Constant Heavy 2 (CH2) cys

2501 GTACGTGAC GCGGTGGAGG TGCATAATGC CAAGACAAG CCGCGGAGG AGCAGTACA CAGCACGTAC CGTGTGTCA CCGTCTCTAC CGTCTGAC  
CATGCACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GGGCCCTCC TCGTCATGTT GTGCTGCATG GCACACCACT CGCAGGAGTG GCAGGACGTG  
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H  
^CH2 cys

2601 CAGGACTGGC TGNATGGCAA GGAGTACAAG TGCAAGTCT CCAACAAGC CCTCCCAGC CCCATCAGA AAACATCTC CAAAGCCAA GGGCAGCCCC  
GTCTGACCG ACTTACCGT CCTCATGTC ACGTTCAGA GGTGTTTCG GGAGGTCGG GGTAGTCTT TTGTAGAG GTTTCGGTTT CCCGTGGGG  
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R  
^CH2 cys

2701 GAGAACCAACA GGTGTACACC CTGCCCCCAT CCGGGAGA GATGACCAAG AACCAGTCA GCCTGACCTG CCTGGTCAA GGTCTCTATC CCAGGACAT  
CTCTTGGTGT CCACATGAG GACGGGGTA GGGCCCTTCT CTACTGTTTC TTGTTCCAGT CCGACTGAC GACCACTTT CCGAAGATAG GGTTCGTGTA  
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I  
^Constant Heavy 3 (CH3) cys

# FIG. 18D

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2801 CGCGGTGGAG TGGGAGAGCA ATGGGCGAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GGTGGACTCC GACGGCTCCT TCTTCCTCTA CAGCAAGCTC
    GCGGCACCTC ACCTCTCTGT TACCCGTGGG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTCCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGAGGCA CTACGTACTC CGAGACCTGT TGGTGATGTG CGTCTTCTCG GAGAGGAGCA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTG CGCGCGGGCG TTTTATTG TTAACATCATG TTTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCGTACG CTGCGGGAT CTCAGGGATT GCGAGCCAAC GCGGCGCCGC AAAAAATAAC AATTGAGTAC AAACGTGTGA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator
    ^start of tet resistance promoter ^-35 of promoter

3101 AAGCTTTTAA GCGTAGTTT ATCAGAGTTA AATTGCTAAC GCAGTCAGGC ACGGTGTATG AAATCTAACA ATGCGCTCAT CGTCATCTC GGCACCGTCA
    TTGGAATTA CGCATCAAA TAGTGTCAAT TTAACGATTG CGTCAGTCGG TGGCACATAC TTAGATTGT TACCGGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation

3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCACGA
3301

```

## FIG. 19A

```
1 GAATTCAACT TCTCCATACT ITGGATAAGG AAATACAGAC ATGAAAAATC TCATTGTCTG GTTGTTATTT AAGCTTGCC AAAAAGAAGA AGAGTCGAAT
  CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
  CTTGACACAC GCCTCCATCT TCGAAACCTC TAATAGCAGT GAGCTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCTCTGA CGACGATAGG GAGCTGTCTG GCGATTAGCT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
  CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTGACGAGG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTACG GCGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTTGTAATA GTACGCCAAGT
  TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGCTA CGCTGATATC
  AGTGCATTTT TCCCATAGAT CTTAATACCT CTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
  1 M K K N I A F L L A S M F V F S I A T N A Y A D I
  ^STII Signal TIR -1 Anti-VEGF Light chain (version Y0317)^

501 CAGTGAACC AGTCCCGGAG CTCCTGTGTC GCCTGTGAG GCGATAGGT CACCATACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
  GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTTA CTTACCTCC TCCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
  TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
  CCTAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGGTTGAA TAATGACAGT TGTCTATATCG TGGCAGCGCA CCGCAAAACC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
  TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCAACT TTAGACCTTG ACCAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCCGA GAGGCCAAG TACAGTGGAA GGTGATAC GCCTCCAT CCGGTAATCT CAGGAGAGT GTCACAGAGC AGGACAGCAA
  ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
```



FIG. 19B

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAGCAGACT ACGAGAAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGGCCTGAGC  
CCTGCTGTTG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGACAGCTTC AGTGGGTAGT CCGGACTCG  
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
1101 TCGCCCGTCA CAAAGAGCTT CAAACAGGGA GAGTGTTAAT TAAATCTCT AGCCCGGAGC CATCGTGGG AGTCGGTAC CCGGGATCT AGGCCTAACG  
AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTTAGGAGA TGCGGCCCTG GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCGGGATTGC  
226 S P V T K S F N R G E C O  
1201 CTCGGTTGCC GCGGGCGT TTTTATTGTT GCGGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT  
GAGCCAACGG CGGCCGCAAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG AGTTACGAA  
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGCTGTAC GAGTAAAGC CGATGCCAG CATTCCTGAC GACGATACGG  
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CGCGACATG CTCCATTTGC GGCTACGGTC GTAAAGGACTG CTGCTATGCC  
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCCTCAGTAA AAGTTAATC TTTCACACAG CTGTCAATAA GTTGTCACGG CCGAGACTTA  
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT  
1501 TAGTCGCTTT GTTTTATTT TTAAATGTAT TTGTAACTAG TAGCCAAGTT CACGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTCTCTCT  
ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATATCTC TTCTTATAGC GTAAAGAAGA  
M K K N I A F L L  
1 ^STII Signal TIR-1  
1601 TGCACTATG TTGTTTTTTT CTATTGCTAC AAACGGCTAC GCTCAGGTC AGCTGGTGA GTCGTGGCA GAGGTGAAA AGCCAGGGC TTCAGTTAAA  
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGAGTCCAAG TCGACCCAGT CAGACCCGCT CTCACCTTTT TCGTCCCGC AAGTCAATTT  
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K  
^Anti-VEGF (version Y0317) Heavy Chain  
^Heavy Chain FR1 changed to SubgroupI consensus sequence  
1701 GTATCCTGTA AAGCTTCTGG CTACGACTTC AGCACTACG GTATGAAGT GGTCCGTGAG GCCCGGGTA AGGGCTTGA ATGGTTTGA TGGAATTAACA  
CATAGGACAT TTGGAAGACC GATGCTGAG TGGGTGATG CATACTTGAC CCAGGCGATC CGGGGGCCAT TCCCGGACCT TACCCAACT ACCTAATGT  
43 V S C K A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T  
1801 CCTATACCGG TGAACCGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGA TACCTGCAGA TGAACAGCCT  
GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGT TTCGTGCTGT ATGGACGCT ACTTGTGCGA  
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L  
1901 GCGGCTGAG GACACTGCG TCTATTACTG TGCAAGTAC CGTACTATT ATGGACGAG CCACTGTAT TTCGACGCT GGGGTCAAG AACCTGGTC  
CGGCGACTC CTGTGACCGC AGATAATGAC AGTTTCTATG GGCATGATAA TACCCTGCTC GGTGACATA AAGTGCAGA CCCCAGTTCC TTGGGACCAG  
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V  
2001 ACCGTCTCT CCGCCTCCAC CAAGGGCCCA TGGTCTTCC CCTGGCACC CTCCTCCAAG AGCACCTCTG GGGGCACAGC GGGCCTGGGC TGCCTGGTCA  
TGCAGAGA GCGGAGGT GTTCCCGGT AGCACAAGG GGGACCGTGG GAGGAGTTC TCGTGGAGC CCCCCTGTG CCGGACCCG ACGGACCACT  
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

# FIG. 19C

2101 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGAACATC AGGCGCCCTG ACCAGCGGG TGACACACCTT CCGGCTGTC CTACAGTCCT CAGGACTCTA  
TCCTGATGAA GGGCTTGGC CACTGCCACA GCACCTTAG GCACCTTAG TCCGCGGAC TGGTCGCCG ACCTGTGGA GGGCCGACAG GATGTCAGG GTCTTGAGAT  
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y  
2201 CTCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG  
GAGGAGTCG TCGCACCACT GACACGGGAG ATCTGCGAAC CCGTGGGTCT GGATGTAGAC GTTGACATTA GTGTGCGGT CGTGTGTT CCACCTGTTT  
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K  
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACCGTGCC AGCACCTGAA CTCCTGGGG GACGTCAGT CTTCTCTTTC CCCCCAAAC  
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACGG GTGGACGGG TCGTGACTT GAGACCCCTC CTGGCAGTCA GAAGGAGAAG GGGGTTTTG  
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P  
2401 CCAAGGACAC CTTATGATC TCCCGGACC CTGAGGTAC ATGCGTGGT GTGACGTGA GCCACGAAGA CCTGAGGTC AAGTTCACT GGTACGTGGA  
GGTTCTGTG GGAGTACTAG AGGCTTGGG GACTCCAGT TACGACAC CACTGCACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT  
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D  
2501 CGCGTGGAG GTGCATAATG CCAAGACAA GCCGCGGAG GAGCAGTACA ACAGCACGTA CCGTGTGGT AGCTCTCTCA CCGTCTTGA CCAGGACTGG  
GCCGACCTC CACGTATTAC GGTCTGTTT CGCGCCCTC CTCGTCACT GTGCTGCACT GGCACACCAAG TCGCAGGAGT GGCAGGACGT GGTCTTGGC  
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W  
2601 CTGATGGA AGGATACAA GTGCAAGTC TCCATCCAG CCGTCCAGC CCGTCCAGT AAGACCATCT CCAAGCCAA AGGCGAGCC CGAGAACCAC  
GACTTACCTG TCCTCATGTT CACGTCCAG AGGTGTTTC GGGAGGTCG GGGTAGCTC TTTTGGTAGA GGTTCGGTT TCCCGTCGG GCTCTTGGT  
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q  
2701 AGGTGTACAC CTTGCCCCA TCCCGGGAAG AGATGACCA GAACAGGTC AGCTGACCT GCCTGGTCAA AGGTCTCTAT CCGAGCGACA TCGCCGTGGA  
TCCACATGT GGACGGGGT AGGCCCTTC TCTACTGTT TCTACTGTT CTTGCTCCAG TCGACTGGA CGGACCACT TCCGAAGATA GGTGCTGT AGCGCACCT  
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E  
2801 GTGGAGAGC AATGGGAGC CGGAGAACAA CTACAGACC AGCTCTCCG TGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC  
CACCTCTCG TTACCGTCG GCCTCTGTT GATGTTCTG TCGGAGGGC ACAGCTGAG CTTGCCGAGG AAGAAGGAGA TGTCTTCA GTGCGACCTG  
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D  
2901 AAGAGAGGT GGCAGCAGG GAACGTCTTC TCATGCTCCG TGATGCATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA  
TTCTGTCCA CCGTCTGCC CTTGCAGAA AGTAGCAGG ACTAGTACT CCGAGACGTG TTGTGATGT GCGTCTTCTC GGAGAGGAG AGAGCCCAT  
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K  
3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACCTGCTGT GCTTCTTCT GTTAACTCAT GTTGTACAGC TTATCATCGA TAAGCTTTAA  
TTATTCGTAC GCTGCGGGA TCTCAGGAT TCGAGCCAA CGGCGGCCCG CAAAAATAA CAATTGAGTA CAACCTGTG AATAGTAGCT ATTGAAAT  
477 O  
3101 TCGGTAGTT TATCAGATT AATTGCTAA CGCAGTCAG CACCTGTAT GAATCTAAC AATGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG  
ACGCCATCAA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGGACATA CTTTAGATTG TTACCGAGT AGCAGTAGGA GCCGTGGCAG TGGACCTAC

\*Start Tet Resistance Coding Sequence

## FIG. 19D

3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGGCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAC TATGGCGTGC TGCTAGCGCT  
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGTCAGTG ATACCGCAGG ACGATCGCGA

3301

FIG. 20A

1 GAATTCAACT TCCTCATACT ITGGATAAGG AAATACAGAC ATGAAAAATC TCATTGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCTGTCCTT TCTCAGCTTA  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCTGTCCTT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG AATTATCGTCA CTGCAATATG TCGCAAAATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CCGGTTTTAC TGGTGTGCGC CAACTAACTA GTCCATCTCC

201 GGGGCGCTGA CGAGGTAAG CCGATGCCA GCATTCTCTGA CGACGATACG GAGTGTCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA  
CCCGGACAT GCTCCATTTC GGGTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACCA GCTGTCAATA AGTTGTACAG GCGAGACTT ATAGTCGCTT TGTCTTTTAT TTTTAATGTA TTTGTAACTA GTACGCAAGT  
TTTTCAAATTA GAAAGTTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGTATCTTA GAATTATGAA GAAATATATC GCATTCTCTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC  
AGTGCATTTT TCCCATAGAT CTTAATACIT CTTCTTATAG CGTAAAGTAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K N I A F L L A S M F V F S I A T N A Y A D I  
^STII signal TIR-1 anti-IgE light chain^

501 CAGCTGACCC AGTCCCCGAG CTCCTGTGCC GCCTCTGTGG CGCATAGGCT CACCATCACC TGCCGTGCCA GTCAGAGCGT CGATTACGAT GGTGATAGCT  
GTCGACTGGG TCAGGGGCTC GAGGACACCG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGGCACGGT CAGTCTCGCA GCTAATGCTA CCACTATCGA

26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y

601 ACATGAACCTG GTATCAACAG AAACCAGGAA AAGCTCCGAA ACTACTGATT TACGCGGCTT CGTACCTGGA GTCGTGAGTC CCTTCTCGCT TCTCTGGATC  
TGTAATTGAC CATAGTTGTC TTTGGTCCCTT TTCAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACCT CAGACCTCAG GGAAGAGCGA AGAGACCTAG

60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S

701 CGGTTCTGGG ACGGANTTCA CTCTGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAAATC ACGAGGATCC GTACACATTT  
GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC GTCGCGCTTC TGAAGCGTTG AATATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAT

93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F

801 GGACAGGTA CCAAGGTGA GATCAAAACGA ACTGTGGCTG CACCATCTGT CTTTCATCTC CCGCATCTG ATGAGCAGTT GAAATCTGA ACTGCTCTG  
CCTGTCCCAT GGTTCACCT CTAGTTGCT TGACACCGAC GTGGTAGACA GAACTAGAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC

126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

901 TTGTGTGCTT GCTGAATAAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGTGGATA ACGCCTCCA ATCGGTAAC TCCAGGAGA GTGTACAGA  
AACACACGGA CGACTTATTG AAGATAGGCT CTCTCCGTT TCATGTCACC TTCCACCTAT TCGCGGAGT TAGCCCATTT AGGTCCTCT CACAGTGTCT

160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 20B

1001 GCAGGACAGC AAGACAGCA CCTACAGCCT CAGAGCACC CTGACGCTGA GCAAGCAGA CTACGAGAAA CACAAAGTCT ACGCTGCGA AGTCACCCAT  
CGTCTGTGCG TTCCTGTGCT GGATGTCGGA GTCTGCTGG GACTGCGACT CGTTCTCTTT GATCTCTTT GTGTTTCAGA TGGGACGCT TCAGTGGGTA  
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H

1101 CAGGSCCTGA GCTGCCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTAGCCCGGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT  
GTCCCGGACT CGAGCGGGCA GTGTTCTTCG AAGTGTGCC CTCTCACAAAT TAAATTAGGA GATCGGCGCT GCGTAGCACC GCTCGAGCCA TGGGCCCTTA  
226 Q G L S S P V T K S F N R G E C O

1201 CTAGSCCTAA CGTCTGGTGG CCGCCGGGCG TTTTATTG TTGCCGACGC GCATCTCGAA TGAATGTGT GCGCAGGTAG AAGCTTTGGA GATTATCGTC  
GATCCGGATT GCGAGCCAAC GCGGCCCGC AAAAATAAC AACGCTGGC GGTAGAGCTT ACTTGACACA CCGTCCATC TTCGAAACCT CTAATAGCAG

1301 ACTGCAATGC TTCGCAATAT GCGCAAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGCGCTGT ACGAGGTAA GCGCATGCC AGCATTCCTG  
TGACGTTACG AAGGTTATA CCGGTTTTTA CTGGTTGTG CCAACTAAT AGTCCATCTC CCCCAGGACA TGCTCCATTT CCGGCTACCG TCGTAAGGAC

1401 ACGAGCATAC GGAGTGCTG CGGATTACG TAAAGAAGTT ATTGAAGCAT CTTGCTCAGT AAAAGTTAA TCTTTTCAAC AGCTGTCTATA AAGTTGTAC  
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTCTTTCAA TAACTTCGTA GGACAGTCA TTTTTCAAIT AGAAAAGTTG TCGACAGTAT TTCAACAGTG

1501 GGCCGAGACT TATAGTCGCT TTGTTTTTAT TTTTAAATGT ATTGTAATGT AGTAGGCAAG TTCAAGGTAA AAGGTATCT AGAATTATGA AGAAGAATAT  
CCGGCTCTGA ATATCAGCGA AACAAAATA AAAAATTACA TAAACATTGA TCATGCGTTC AAGTCAITTT TTCCCATAGA TCTTAATACT TCTTCTTATA  
M K K N I  
^STII Signal TIR-1

1601 CGCAATTCCT CTTGCATCTA TGTTGTTTTT TTCTATTGCT ACAACGCGT ACGTGAAGT TCAGCTGGTG GAGTCTGGG GTGGCCTGCT GCAGCCAGGG  
GCGTAAAGAA GAACGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGCGA TGGACTCCA AGTCGACCAC CTCAGACCGC CACCGGACCA CGTCGGTCCC  
6 A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G  
^anti-IgE heavy chain

1701 GGCTCACTCC GTTGTGCTG TGCAGTTTCT GGCTACTCCA TCACCTCCG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGTAAAGGC CTGGAATGGG  
CCGAGTGAGG CAACAGGAC ACGTCAAGA CCGATGAGT AGTGGAGCC TATATCGACC TTGACCTAGG CAGTCCGGGG CCCATTCCCG GACCTTACCC  
39 G S L R L S C A V S G Y S I T S G Y S W N W I R Q A P G K G L E W V

1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACCC TAGGTCGTAAG GCGCGTATCA CTATAAGTCG CGAGGACTCC AAAAACACAT TCTACCTGCA  
AACGTAGCTA ATGCATACG CCTAGCTGAT TGATATTGG ATCCAGTTC CCGCATAGT GATATTCAGC GCTGCTGAGG TTTTGTGTA AGATGGACGT  
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q

1901 GATGAACAGC CTGCTGTGCT AGGACACTGC CGTCTATTAT TGTGCTCGAG GCAGCCACTA TTTGCGTCA TGGCACTTCG CCGTGTGGG TCAAGGAACC  
CTACTGTGCG GACGACGAC TCCTGTGACG GCAGATAATA ACAGAGCTC CGTGGTGAT AAAGCCAGTG ACCGTGAAGC GGCACACCCC AGTTCCTTGG  
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T

2001 CTGCTCACCG TCTCTCTGCG CTCACCAAG GGCCCATCGG TCTTCCCCCT GGCAACCCTCC TCCAAGAGCA CCTCTGGGG CACAGCGGCC CTGGGCTGCC  
GACCAGTGC AGAGAGCGG GAGGTGGTTC CCGGTAGCC AGAAGGGGA CCGTGGGAGG AGGTCTCTCGT GGAGACCCC GTGTGCGCCG GACCCGACCG  
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

## FIG. 20C

2101 TGGTCAAGGA CTACTTCCC GAACGGTGA CGGTGTCGTG GAACTCAGGC GCGCGGTGA CACTTCCCG GCTGTCCTAC AGTCTCAGG  
ACCAATTCTT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CCGGACACCT GTGGAAGGSC CGACAGGATG TCAGGAGTCC  
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G

2201 ACTCTACTCC CTCAGCAGC TGGTGACTGT GCGCTCTAGC AGCTTGGGCA CCGAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG  
TGAGATGAGG GAGTCGTGCG ACCACTGACA CCGGAGATCG TCGAACCCGT GGTCTGGAT GTAGACGTG CACTTAGTGT TCGGTCGTT GTGGTTCCAC  
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V

2301 GACAAAGAAAG TTGAGCCCAA ATCTTGAGAC AATACTCACA CATGCCACC GTGCCCAGCA CTTGAACCTC TGGGGGACC GTGAGTCTTC CTCTTCCCCC  
CTGTTCTTTC AACTCGGGTT TAGRACACTG TTTTGAGTGT GTACGGGTGG CACGGTCTGT GACTTGAGG ACCCCCTGG CAGTCAGAAG GAGAAGGGG  
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P

2401 CAAACCCCAA GGACACCCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGGTGGTGG ACCTGAGCCA CGAAGACCCCT GAGTCAAGT TCAACTGGTA  
GTTTGGGTT CCTGTGGAG TACTAGAGG CCTGGGACT CCACTGTAAG CACCACCACC TGCACTCGGT GCTTCTGGA CTCAGTTCA AGTTGACCAT  
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y

2501 CGTGACGGC GTGAGGTGC ATATGCCAA GACAAAGCG CCGGAGGAGC AGTACAACAG CAGTACCGT GTGGTCAGCG TCCTACCGT CTGCACACAG  
GCACCTGCC CACCTCCACG TATTACGGTT CTGTTTCGGC GCGTCTCTCG TCATGTTGTC GTGCATGGCA CACCACTGCG AGGAGTGGCA GGAGTGGTC  
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q

2601 GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGTCTCCA ACAAGCCCT CCAGCCCCC ATCAGAAARA CCATCTCCA AGCCAAAGG CAGCCCCGAG  
CTGACCGACT TACCGTTCT CATGTTACG TTCCAGAGGT TGTTTCGGA GGTCGGGG TAGTCTTTT GTAGAGGTT TCGGTTTCC GTGGGGGTC  
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E

2701 AACCAACAGT GTACACCCCTG CCCCATCCC GGGAAAGAGT GACCAAGAAC CAGTACAGC TGACCTGCGT GGTCAAAGGC TTCTATCCA GCGACATCGC  
TTGGTGTCCA CATGTGGAC GGGGTAGG CCGTCTCTA CTGTTCTTG GTCCAGTCGG ACTGGACGGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG  
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A

2801 CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GAACAACATC AAGACCACGC CTCGCGTGT GGACTCCGAC GGCTCTTCT TCCTCTACAG CAAGCTCACC  
GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTCTGTGATG TTCTGGTGG GAGGCGACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG  
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F L Y S K L T

2901 GTGACAAGA GCAGTGGCA GCAGGGGAAC GTCTTCTCAT GTCCTGTGAT GCATGAGGT CTGCACAAAC ACTACACGCA GAAGAGCCTC TCCTGTCTC  
CACCTGTTCT CGTCCACCGT CGTCCCTTG CAGAAAGTA CGAGCACCTA CGTACTCGA GAGTGTGG TGATGTGGT CTCTCGGAG AGGACAGAG  
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P

3001 CGGGTAAATA AGCATGCGAC GGCCTTAGAG TCCCTAACGC TCGGTTGCC CCGGGCGTTT TTTATTGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG  
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTTGG AGCCAACGCG GGCCCGCAAA AATAACAAT TGAGTACAAA CTGTGGAATA GTAGCTATT  
473 G K O

3101 CTTTAATGCG GTAGTTTATC ACAGTTAAAT TGCTAACGCA GTACGGCACC GTGTATGAA TCTAACAAAT CGCTCATCGT CATCTCGGC ACCGTACCC  
GAATACCG CATCAATAG TGTCAAATTA ACGATTGCGT CAGTCCGTGG CACATACCTT AGATTGTTAC GCGAGTACGA GTAGGAGCGG TGGCAGTGG

## FIG. 20D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCCTCTTG CGGGATATCG TCCATTCCGA CAGCATCGCC AGTCACTATG GCGTGCTGCT  
ACCTAGGACA TCCGTATCCG AACCAATACG GCCATGACGG CCCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCACGACGA  
3301

## FIG. 21A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATATACAGAC ATGAAAAATC TCATTGGCTGA GTTGTATT TT AAGTTGCC AAAAAGAAGA AGAGTCGAAT  
CITTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGTCTG TACTTTTATG AGTAACGACT CAACAATAAA TTTCGAACGGG TTTTTCCTCT TCTCAGCTTA  
101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTCGAATGCT TCGCAATATG GCGCAAAATG ACCAAACAGCG GTTGATTGAT CAGGTAGAGG  
CITGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTIACGA AGCGTTATAC CGCGTTTATC TGGTGTGCG CAACATACTA GTCCATCTCC  
201 GGGCGCTGTA CGAGGTAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGCTGTCTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACGTA  
CCGCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT  
301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAAG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTGTAACCTA TTACGCAAGT  
TTTTCAAITTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA  
401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCTA CGCTGATATC  
AGTGCAITTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG  
1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
^StII signal TIR-1 anti-IgE light chain^  
501 CAGCTGACCC AGTCCCCGAG CTCCTGTCC GCCTCTGTGG GCGATAGGTT CACCATACC TGCCGTGCCA GTCAGAGCGT CGATTACGAT GGTGATAGCT  
GTCGACTGGG TCAGGGGGCTC GAGGACACAG CGGTATCCCA GTGGTAGTGG ACGGCACGGT CAGTCTCGCA GCTAATGCTA CCACTATCGA  
26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y  
601 ACATGAACCTG GTATCAACAG AAACCCAGGAA AAGTCCGAA ACTACTGATT TACGCGGCTT TACGACCTGA GTCTGGAGTC CTTTCTCGCT TCTCTGGATC  
TGTTACTTGAC CATAGTTGTC TTTGGTCCCTT TTCGAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACCT CAGACCTCAG GGAAGAGCGA AGAGACCTAG  
60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S  
701 CGGTTCTGGG ACGGATTTCA CTCGTACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAAATC ACGAGGATCC GTACACATTT  
GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTGCTCAGAC GTGCGCTTC TGAAGCGTTG AATAATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAA  
93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F  
801 GGACAGGGTA CCAAGGTGGA GATCAAAACGA ACTGTGGCTG CACCATCTGT CTTCACTTTC CCGCATCTG ATGAGCAGTT GAAATCTGA ACTGCCCTG  
CCTGTCCCAT GGTTCACCT CTAGTTTGTG TGACACCGAC GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC  
126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V  
901 TTGTGTGCCT GCTGAATAAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCAGGAGA GTGTCACAGA  
AACACACGGA CGACTTATTG AAGATAGGCT CTCTCCGTT TCATGTCAAC TTCCACCTAT TCGGGGAGT TAGCCCAITG AGGTCCTCT CACAGTGTCT  
160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E



FIG. 21B

1101 GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC CTGACGCTGA GCAAGAGAGA CTACGAGAAA CACAAAGTCT AGCCTTGCGA AGTCACCCAT  
CGTCTGTCTG TTCTGTCTGT GATGTCTGG GACTGCGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TGGGAGCGCT TCAGTGGGTA  
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H  
1101 CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCCGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT  
GTCCCGGACT CGAGCGGCA GTGTTTCTCG AAGTGTGCC CTCTACAAAT TAATTAGGA GATCGGCGCT GGTAGCACC GCTCGAGCCA TGGGCCCCCTA  
226 Q G L S S P V T K S F N R G E C O  
1201 CTAGGCTTAA CGTCTGGTGG CGCCCGGGCG TTTTCTATTG TTGCCGAGCG GCATCTCGAA TGAATCTGTG GGCAGGTAG AAGCTTTTGA GATTATCTGC  
GATCCGGATT GCGAGCCAAC GCGGCGCCGC AAAAATAAAC AACGGCTGCG CGTAGAGCTT ACTTGACACA CGCGTCCATC TTCGAAACCT CTAATAGCAG  
1301 ACTGCAATGC TTCGCAATAT GCGCAAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGGCGCTGT ACAGGTAAA GCCCGATGCC AGCATTCCTG  
TGAGTTACG AAGGTTATA CCGGTTTGA CTGGTTGTCG CCACTAAT AGTCCATCTC CCCCAGGACA TGCTCCATTT CCGGCTACGG TCGTAAGGAC  
1401 ACAGCATAC GGAGCTGCTG CCGGATTACG TAAAGAAAT ATTGAAGCAT CCTCGTCACT AAAAAGTTAA TCTTTTCAAC AGCTGTCTATA AAGTTGTAC  
TGCTGTATG CCTCGACGAC GCGCTAATGC ATTCTTTCAA TAACTTCGTA GGAGCAGTCA TTTTTCAAAT AGAAAAGTTG TCGACAGTAT TTCAACAGTG  
1501 GCGGAGACT TATAGTCGCT TTGTTTATTT TTTTAAATGT ATTGTAATGT AGTACGCAAG TTCACGTAAA AAGGTAATCT AGRATTATGA AGRAGAAAT  
CCGCTCTGA ATATCAGCGA AAAAAAATA TAAACATTGA TCATCGCTTC AAGTCAATTT TTCCCATAGA TCTTAATATCT TCTTCTTATA  
M K K N I  
1  
^STII Signal TIR-1  
1601 CGCATTTCTT CTTCGATCTA TGTTCTGTTT TTCTATTGCT ACAACGGCT ACCTCAGGT TCAGCTGCNA GAGTCTGGC CGGGCCTGGT GAAACCATCT  
GCGTAAAGAA GAAGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGCGCA TGCAGTCCA AGTCGACGTT CTCAGACCGG GCCCGGACCA CTTTGGTAGA  
6 A F L L A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S  
^anti-IgE Heavy Chain  
^Heavy Chain FR1=SubgroupII consensus sequence  
1701 CAGACTCTCT CTTGACTTG TACTGTTTCT GGCTACTCCA TCACCTCCCG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGGTAAAGGC CTGGAATGGG  
GTCTGAGAGA GGAATGAAC ATGACAAAAG CCGATGAGGT AGTGAGGCG TATATCGACC TTGACCTTAG CAGTCCGGG CCCATTCCCG GACCTTACCC  
39 Q T L S L T C T V S G Y S I T S G Y S W N W I R Q A P G K G L E W V  
1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACCC TAGGTCACAG GGCGTATCA CTATAAGTGC CGACGACTCC AAAAACACAT TCTACCTGCA  
AACGTAGCTA ATGCATACCT CTTAGCTGAT TGATATTGGG ATCGAGTTTC CCGCATAGT GATATTACG GCTGCTGAGG TTTTGTGTA AGATGGAGCT  
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q  
1901 GATGAACAGC CTGGTGTCTG AGGACACTGC CGTCTATTAT TGTCTCGAG GCAGCCACTA TTTTCGGTCA TGGCACTTTC CCGTGTGGGG TCAAGGAACC  
CTACTGTCTG GACGACGAC TCCTGTGACG GCAGATAATA ACACAGCTC CGTCCGTGAT AAAGCCAGT ACCGTGAAGC GGCACACCCC AGTTCCTTGG  
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T  
2001 CTGCTCACCG TCTCTCGGC CTCACCAAG GGCCCATCGG TCTTCCCTCT GGCACTCTCC TCCAAGAGCA CCTTGTGGGG CACAGCGGCC CTGGGCTGCC  
GACCAGTGGC AGAGAGCCG GAGGTGTTTC CCGGTAGCC AGAAGGGGA CCGTGGGAGG AGGTCTCTGT GGAGACCCCG GTGTGCGCCG GACCCGACGG  
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

## FIG. 21C

2101 TGGTCAAGGA CTACTTCCCG GAACCGGTGA CGGTGTCGTG GAACTCAGGC GCCCTGACCA GCGGGGTGCA CACCTTCCCG GCTGTCCTAC AGTCCTCAGG  
ACCACTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGCT GCGCGCACGT GTGGAAGGCG CGACAGGATG TCAGGAGTCC  
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G

2201 ACTCTACTCC CTCAGCAGCG TGGTGAATGT GCCCTTAGC AGTTTGGGA CCAGACCTTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG  
TGAGATGAGG GAGTCGTGCG ACCACTGACA CGGAGATCG TCGAACCCGT GGGTCTGGAT GTAGACGTG CACTTAGTGT TCGGGTCTGT GTGGTTCCAC  
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V

2301 GACAAGAAAG TTGAGCCCAA ATCTTGTGAC<sup>1</sup> ABAACTCACA CATGCCACCA GTGCCACCA CCTGAACCTC TGGGGGGACC GTCAGTCTTC CTCTTCCCCC  
CTGTCTTTC AACTCGGGTT TAGAACACTG TTTTGAATGT GTACGGGTGG CACGGGTCTG GACTTGAGG ACCCCCTGG CAGTCAGAAG GAGAAGGGG  
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P

2401 CAAAACCCAA GGACACCTC ATGATCTCC GGACCCCTGA GGTCAATGC GTGTGGTGG ACCTGAGCCA CGAAGACCTT GAGTCAAGT TCAACTGTGA  
GTTTGGGTT CCTGTGGGAG TACTAGAGG CCTGGGACT CAGTGTAGC CACCAACACC TGCACCTGGT GCTTCTGGA CTCACGTTCA AGTTGACCAT  
273 K P K D T L M I S R T P E V T C V V D V S H E D P E V K F N W Y

2501 CGTGGACGG GTGGAGGTG ATATGCCAA GACAAGCCG CGGAGGAGC AGTACAACAG CAGTACCGT GTGTCAGG TCCTCACCGT CCTGCACAG  
GCACCTGCC CACCTCCACG TATTACGGT CTGTTCGGC GCCCTCCTG TCATGTTGC GTGCATGCA CACCACTGC AGGAGTGCA GACGTTGTC  
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q

2601 GACTGGCTGA ATGCCAAGGA GTACAAGTGC AAGTCTCCA ACAAGCCCT CCAGCCCGC ATCGAGAAA CCATCTCAA AGCAAAGG CAGCCCGAG  
CTGACCGACT TACGTTCTT CATGTTACG KATGTTGAG TGTTCGGA GGTTCGGGG TAGCTCTTT GGTAGAGTT TCGGTTTCCC GTCGGGGCTC  
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E

2701 AACACAGGT GTACACCCCTG CCCCATCCC GGAAGAGAT GACCAAGAAC CAGGTCAGC TGACCTGCTT GGTCAAAGC TTCTATCCA GGCACATCG  
TTGGTGCCA CATGTGGGAC GGGGTAGG CCTTCTCTA CTGTTCTTG GTCCAGTCG ACTGGACCGA CCAGTTTCCG AAGATAGGT CCGTGTAGCG  
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A

2801 CGTGGAGTG GAGAGCAATG GGCAGCCGGA GAACAACCTAC AAGACCAAGC CTCCTGCTGT GACTCCGAC GGCTCTTCT TCTCTACAG CAAGCTCACC  
GCACCTCACC CTCTCGTTAC CCGTCGGCT CTGTGTTATG TTCTGGTGG GAGGGCACA CCGAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG  
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T

2901 GTGACAAGA GCAGGTGGA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGCT CTGCACAACC ACTACACGA GAAGAGCTC TCCCTGTCTC  
CACCTGTTT CGTCCACCGT CGTCCCTTG CAGAAAGTA CGAGCACTA CGTACTCGA GAGGTGTTG TGATGTGCT CTCTCGAG AGGACAGAG  
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P

3001 CGGTAATAA AGCATGCGAC GGCCCTAGAG TCCTTAAGC TCGGTTGCG CCGGCGGTTT TTTATGTTA ACTCATGTT GACAGCTTAT CATCGATAAG  
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTCGG AGCCAACGGC GGGCCGCAAA AATAACAAT TGAGTACAAA CTGTGGAATA GTAGCTATTC  
473 G K O

3101 CTTTAATGG GTAGTTTATC ACAGTTAAAT TGTAACCGA GTCAAGCACC GTGTATGAA TCTAACATG CGCTCATGT CATCTCGG ACCGTCAACC  
GAAATTACG CATCAATAG TGTCAAITTA ACAGTTGGT CAGTCCGTTG CACATCTTT AGATTGTTAC GCGAGTAGCA GTAGGAGCCG TGGCAGTGGG

## FIG. 21D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCCTCTTG CCGGATATCG TCCATTCCGA CAGCATCGCC AGTCACTATG GCGTGCTGCT  
ACCTACGACA TCCGTATCCG AACCAATACG GCCATGACGG CCCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGGACGA

3301

## FIG. 22A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGGCC AAAAAGAAGA AGAGTCGAAT  
CTTAAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTCA CTGCAATGCT TCGCAATPAT GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAAC TA GTCCAICTCC

201 GGGCGCTGA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACGTA  
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACA GCTGTCAFAA AGTTGTACG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTTGTAAC TA GTACGCAAGT  
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC  
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTCGCGAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
^STII Signal TIR -1 anti-VEGF Light Chain (1st generation)^

501 CAGATGACCC AGTCCCGGAG CTCCTGTGTC GGTCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACCTGGT  
GTCTACTGGG TCAGGGGCTC GAGGACACAG CGCTATCCCA GTGGTAGTGG AGCTCGCGTT CAGTCCCTATA ATCGTTTGATA AATTGACCA

26 Q M T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAC  
TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGTTACC  
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCAATCG TGGCACGSCA CCTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC  
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCTCCCAAT CCGGTAATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

## FIG. 22B

1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAACAGAGACT ACAGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC  
CCTGTGCTGG ATGTGGAGT CGTGTGGGA CTGGGACTCG TTTCGTCTGA TGCTCTTGT GTTCAGATG CGACGCTTC AGTGGTACT CCGGACTCG  
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
1101 TCGCCCGTCA CAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCTCT ACGCCGAGC CATCTGGG AGCTCGGTAC CCGGGATCT AGGCCTAACG  
AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTGCAAAATTA ATTTAGGAGA TCGGGCCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC  
226 S P V T K S F N R G E C O  
1201 CTGGTTGCC GCGGGCGT TTTTATTGT GCGAGCGC ATCTGGAATG AACTGTGTC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCATATGCTT  
GAGCCAACG CGGCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACCTTACGAA  
1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGGG GCGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG  
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGGACATG CTCATTTCC GGCTACGGTC GTAAGGACTG CTGCTATGCC  
1401 AGTCTGCTCG CGATTACGTA AAGAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTACCG CCGAGACTTA  
TCGACGACG GCTAATGCAT TTCTTCAATA ACTTCGTAG AGCAGTCAIT TTTCAAITAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT  
1501 TAGTGCCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT  
ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCCATAGATC TTATATACITC TTCTTATAGC GTAAAGAAAGA  
1 M K K N I A F L L  
1 ^STII Signal TIR-1  
1601 TGCATCTATG TTCTTTTTT CTATTGCTAC AAACGGTAC GCTGAGTTC AGCTGGTGA GTCTGGCGT GGCCTGGTGC AGCAGGGGG CTCACCTCGT  
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTCGCGATG CGACTCCAAG TCAGCCACCT CAGACCGCA CCGGACCAAG TCGTCCCTCC GAGTGAGCA  
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
^anti-VEGF (1st generation) heavy chain  
1701 TTGTCTGTG CAGCTTCTGG CTATACCTTC ACCAATATG GTATGAATG GTTCCGTGAG GCGCCGGGTA AGGGCTTGA ATGGTTTGA TGGATTACA  
AACAGGACAC GTCAAGACC GATATGGAAG TGTTTGATAC CATACTGAC CCAGGCGATC CCGGGCCCAT TCCGGGACCT TACCCAACT ACCTAAITGT  
43 L S C A A S G Y T F T N Y G M N W V R Q A P G K G L E W V G W I N T  
1801 CCTATACCGG TGAACCGACC TATGCTGCGG AITTCAAAAG TCGTTTCACT TTCAAGCTTAG ACACCTCCAA GTGACAGCA TACCTGCAGA TGAACAGCCT  
GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAGTCGAATC TGTGGAGTT TGTGGAGTT CAGCTGTCTGT ATGACAGTCT ACTTGTGGA  
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L  
1901 GCGTGTGAG GACACTGCCG TCTATTACTG TGCAAGTAC CCCCATAAT ATGGGAGCAG CCACTGGTAT TTGACGCTCT GGGGTCAAGG AACCTGTGTC  
CGCAGGACTC CTGTGACGCG AGATAATGAC ACGTTTCTAG GGGGTGATAA TACCCTCGTC GGTGACCATTA AAGCTGCAGA CCCAGTTCC TTGGGACGAG  
110 R A E D T A V Y Y C A K Y P H Y Y G S S H W Y F D V W G Q G T L V  
2001 ACCGTCTCT CGGCTCCAC CAAGGGCCCA TCGTCTTCC CCGTGGCACC CTGCTCCAAG AGCACCTCTG GGGGCACAGC GGCCTGGGC TGCCTGGTCA  
TGGCAGAGGA GCGGAGGTG GTTCCCGGGT AGCAGAAAG GGGACCGTGG GAGGAGTTTC TGTGGAGATC CCGGTGTG CCGGACCGG ACGGACCACT  
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

## FIG. 22C

2101 AGGACTACTT CCCCAGACCG GTGACGGTGT CGTGGAACTC AGCGGCCCTG ACCAGCGGGG TGCACACCTT CCGGCTGTC CTACAGTCTT CAGGACTCTA  
TCCTGATGAA GGGCTTGGC CACTGCCACA GCACCTTGAG TCGCGGGAC TGCTGCCGC ACCTGTGGA ACCTGTGGA GGGCCGACAG GATGTGAGG GTCTGTAGAT  
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCTGGTGA CTGSCCCTC TAGCAGCTTG GGCACCCAGA CTTACATCTG CAAAGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG  
GAGGAGTCG TCGCACCCT GACACGGGAG ATGCTCGAAC CCGTGGGTCT GGATGTAGAC GTTGACACITTA GTTTCGGGT CGTTGTGGTT CCACCTGTTC  
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACCGTGCC AGCACCTGAA CTCCTGGGG GACCGTCAGT CTTCTCTTC CCCCCAAAAC  
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACG GTGCACGGG TCGTGACTT GAGGACCCCT CTGCGAGTCA GAAGGAGAAG GGGGGTTTG  
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CTTATGATC TCCGGACCC CTGAGGTGAC ATGCGTGGT GTGGACGTGA GCCACGAAGA CCTGAGGTC AAGTTCAACT GGTACGTGGA  
GGTTCTCTGT GGAGTACTAG AGGSCCTGG GACTCCAGT TAGCCACCAC CACTGCACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACTT  
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

2501 CGCGTGGAG GTGCATAATG CCAAGACAAA GCCCGGGAG GAGCAGTACA ACAGCACGTA CCGTGTGTC AGCGTCTCTCA CCGTCTCTCA CCAGGACTGG  
GCCGACCTC CACGTATTAC GGTCTGTTT CGCGCCCTC CTGCTCATG TGTGTCATG GGCACACCAG TCGCAGGAGT GGCAGGAGT GGTCTCTGAC  
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W

2601 CTGAATGGCA AGGATACAA GTGCAAGTC TCCAACAAAG CCTCTCCAGC CCCCATCGAG AAAACCATCT CCAAAGCCAA AGGCGAGCC CGAGAACCAC  
GACTTACCGT TCCTCATGTT CAGTTCCAG AGTTGTTTC GGGAGGTCG GGGTAGCTC TTTTGGTGA GGTTCGGT TCCCGTCGG GCTCTTGGT  
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q

2701 AGGTGTACAC CTTGCCCCCA TCCCGGGAAG AGATGACCAA GAACAGGTC AGCTGACCT GCCTGGTCAA AGGCTTCTAT CCCAGCGACA TCGCCGTGGA  
TCCACATGT GAGCGGGGT AGGCCCTTC TCTACTGTT CTGTGTCAG TCGACTGGA CGGACCATGT TCCGAAGATA GGTCTGCTGT AGCGCACCT  
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E

2801 GTGGAGAGC AATGGGCAGC CGGAGAACAA CTACAAGAC ACCTCTCCG TGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC  
CACCTCTCG TTACCCGTCG GCCTCTTGT GATGTTCTG TCGGAGGGC ACACCTGAG GCTGCCGAGG AAGAAGGAGA TGTGTTTGA GTGCGACCTG  
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D

2901 AAGACAGGT GGCAGCAGG GAAGTCTTC TCATGCTCG TGATGCATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA  
TTCTGTTCA CCGTGTGCC CTTGCAGAG AGTACGAGC ACTACGTACT CCGAGACGTG TTGCTGATGT GCGTCTTCTC GGAGAGGGAC AGAGGCCCAT  
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

3001 AATAAGCAT CGACGGCCCT AGAGTCCCTA ACCTCTGTT CCGCCCGGC GTTTTTTATT GTTAACTCAT GTTTGACAGC TTATCATCGA TAAGCTTTAA  
TTATTCGTAC GCTGCCGGA TCTCAGGGAT TCGAGGCCAA CGCGGCCCG CAAAANATRA CAATTGAGTA CAACTGTCTG AATAGTAGT ATTGGAAT  
477 O

3101 TCGGTAGTT TATCAGATT AATTTGCTAA CGCAGTCAG CACCGTGTAT GAAATCTAAC AATGCGTCA TCGTCATCTT CGGCACCGTC ACCCTGGATG  
ACGCCATCAA ATAGTCAA TTTAACGATT GCGTCAGTCC GTGACACATA CTTAGATTG TTAGCGCAGT AGCAGTAGGA GCCGTGGCAG TGGACCTAC

3201 CTGTAGGCAT AGGCTTGGTT ATGCGGTAT TCGCGGCCT CTTGCCATT ATCGTCCATT CCGACAGCAT CGCAGTCAAC TATGGCGTGC TGCTAGCGCT  
GACATCCGTA TCCGAACCAA TACGCCCATG ACGCCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGTCAAGT ATACCCGAG ACATCCGGA

FIG. 23A

>Anti-VSGF (VNERK version) IgG1 Expression Cassette with heavy chain FR1,2,3,4=consensus subgroup I

ecorI pflMI bsrDI hindIII earI/ksp6321  
1 GAATTCAACT TCTCCATACCT TTGGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTATTAT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

bspMI bsrDI bclI  
101 GAACTGTG CCGAGGTAGA AGCTTGGAG ATTATCTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCTCCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTGCG CAACCTAATA GTCCATCTCC

bsmI snaBI  
201 GGGCGCTGTA CAGAGTAAAG CCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTGAGTA  
CCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

pvuII eagI/xmaIII/ecfXI speI  
301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTACG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAACCTA GTACGCAAGT  
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA

xbal bsiWI/spI mluI ecorV  
401 TCACGTAAAA AGGTTATCTA GAATTATGAA GAAGATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CCGTGTATATC  
AGTGCATTTT TCCCATAGAT CTTAATACTT CTCTCTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCGAT CCGACTATAG  
M K K N I A F L L A S M F V F S I A T N A Y A D I  
^STII Signal TIR -1

estI pstI  
501 CAGTTGACCC AGTCCCGAG CTCCCTGTC GCTCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACCTGGT  
GTCAACTGGG TCAGGGGCTC GAGGACAGG CCGAGACACC CGCTATCCCA GTGCTAGTGG ACCTGCGGTT CAGTCTTATA ATCGTTGATA AATTGACCA  
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

scaI bspMI bamHI  
601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC  
TAGTGTCTT TGGTCTTTT CGAGGCTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTG  
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

^Light chain

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kpnI      asp718      acc65I
701 GGATTTCAC TCGACCATCA GCAGTCTGCA GCCAGAGAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGAGCT CGGTCTCTG AAGCGTTGAA TAATGACAGT TGTATATATCG TGGCAGCGCA CCTGCAAAACC TGTCCCATGG
93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

xmnlI      bpuAI      bbsI
801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTGCTTGG ACACCGAGCT GGTAGACAGA AGTAGAAGG I F P P S D E Q L K S G T A S V V C L L
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

xmnlI      asp700
901 TGAATAACTT CTATCCGAGA GAGGCCAAG TACAGTGGAA GGTGATAAC GCCTCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCGGTTC CTCCGGTTC ATGCACCTT CCACCTATTG CGGAGGTTA GCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

cellI/espI      bspI/bpu1102I
1001 GACAGACACC TACAGCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAGAAACA CAACTCTAC GCCTGCGAAG TCACCCATCA GGGCTCTGAGC
CCTGTCTGG ATGTCGAGT CGTGTGGGA CTGCGACTCG TTGCTCTGA TGCTCTTGT GTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

xmaI/pspAI
1101 TCGCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATCGTGCG AGCTCGGTAC CCGGGATCT AGGCTTAACG
AGCGGAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGGAGA TGCGGCTGC GTAGACCCG TCGAGCCATG GGCCCTAGA TCGGATTCG
226 S P V T K S F N R G E C O

start lambda t0 terminator

bspMI      aviII/fspI      hindIII      bsrDI
1201 CTCGGTGGC GCCGGGCGT TTTTATTGT GCGAGCGGC ATCTCGAATG AACTGTGTC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TGCATGCTT
GAGCCAAAGG CGGCCCGCA AAAATAACAA CGGCTGGCG TAGAGCTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGT ACCTTACGAA
^end lambda t0 terminator

```

FIG. 23B



1301 CCGAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG  
GGGTATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCC CCGGACATG CTCCATTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC bsmI

1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTCACACAG CTGTCATAAA GTTGTACGG CCGAGACTTA  
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGAGG AGCAGTCATT TTTCAAATTAG AAAAGTTGTC GACAGTATT CAACAGTGCC GGTCTCTGAAT pvuII eagI/xmaIII/ecI XI

1501 TAGTGGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGTT CACGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTCCTCT  
ATCAGCGAA CAAAAATAA AAATTACATA AACATTGATC ATGGTTTCAA GTGCATTTT CCCATAGATC TTAATACCTT TCCTATAGC GTAAAGNAGA xbaI  
M K K N I A F L L  
^STII Signal TIR-1

1601 TGCATCTATG TTGTTTTTT CTATTGCTAC AAACGGCTAC GCTCAGGTC AGCTGGTGA GTCTGGCGCA GAGGTGAAAA AGCCAGGGGC TTCAGTTAAA  
AGGTAGATC AAGCAAAAA GATACGATG TTTCGGCATG CGAGTCCAAG TCGACCACGT CAGACCGGT CTCCACTTT TCGGTCCCG AAGTCNAITTT eco57I  
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K  
^start xVEGF(VNERK) heavy chain (consensus subgroup I framework  
^FR1=SubgroupI

43 V S C K A S G Y T F T N Y G I N W V R Q A P G Q G L E W M G W I N T  
^FR2=SubgroupI

1701 GTATCTCTGA AGCTTCTGG CTATACCTTC ACCAATATG GTATAAACTG GTTCCGTCAG GCCCGGGTGC AGGGCTTGA ATGATGGA TGGATTAAACA  
CATAGGACAT TTCAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGCAGTC CCGGCGCCAG TCCCGGACCT TACCTACCCT ACCTAATTGT  
77 Y T G E P T Y A A D F K R R V T I T A D T S T S T A Y M E L S S L  
^FR3=SubgroupI

1801 CCTATACCG TGAACCGACC TAGTCTCGG ATTTCAAACG TCGTGTACT ATCACTGCTG ACACCTCCAC TAGCACAGCA TACATGGAAC TGTCTAGCCT  
GGATATGCC ACTTGGCTGG ATACGACGC TAAAGTTTC AGCAATGA TAGTGACGAC TAGTGAGGTG ATCGTGTGCT ATGTACCTTG ACAGATGGA  
77 Y T G E P T Y A A D F K R R V T I T A D T S T S T A Y M E L S S L  
^FR3=SubgroupI

1901 GCGCTCTGAG GACATGCCG TCTATTACTG TGCAGCTTAC CCGCACTATT ATGTGAACGA CGGAADAGC CACTGGTATT TCGACGCTG GGGTCAAGGA  
CGGAGACTC CTGTGACGG AGATATGAC AGGTGCAATG GCGGTGATAA TACACTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT  
110 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G  
FR4= same sequence for subgroupI, II and III

2001 GCGCTCTGAG GACATGCCG TCTATTACTG TGCAGCTTAC CCGCACTATT ATGTGAACGA CGGAADAGC CACTGGTATT TCGACGCTG GGGTCAAGGA  
CGGAGACTC CTGTGACGG AGATATGAC AGGTGCAATG GCGGTGATAA TACACTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT  
110 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G  
FR4= same sequence for subgroupI, II and III

FIG. 23C

[illegible]

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xmaI/pspAI      bspI407I/bsrDI      sexAI      bspMI      bspMI
smaI earI/ksp632I  AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT
2701 GAGAACACA GGTGTACACC CTGCCCCCAT CCGGGAAGA GATGACCAAG AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT
CTCTTGCTGT CCACATGTG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTGCCAGT CGGACTGGAC GGACCAGITT CCGAAGATAG GGTGCTGTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I

berDI
2801 CGCCCTGGAG TGGGAGACA ATGGGAGCC GGAGAACAAC TACAAGACCA CGCCTCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTA CAGCAAGCTC
GGGCACTC ACCCTCTCT TACCGTGG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L

bpuAI      ppulOI      nsII/avaIII      bspI      earI/ksp632I
xmaI bbsI      asp700
2901 ACCGTGACA AGAGCAGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTGTCCAC CGTGTCCC CTGCAAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGTGTG CGTCTTCTCG GAGAGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S

claiI/bsp106      bspDI
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTG CCGCCGGCG TTTTATTG TTAATCATG TTTGACAGCT TATCATGAT
GAGGCCCAT TATTCGTACG CTGCCGGAT CTCAGGAT GCGAGCCAAC GCGGCCCGC AAAAATAAC AATTGATAC AAATGTCTGA ATAGTAGCTA
477 P G K O      hpaI      bspDI

hindIII
3101 AGCTTTAAT GCGTAGTTT ATCAGATTA AATTGCTAAC GCAGTCAGC ACCGTGTATG AAATCTAACA ATGCGTCAAT CGTCATCCTC GGCACCGTCA
TTGGAATA CGCCATCAA TAGTGTCAAT TTAACGATTG CGTCAGTCCG TGGCACATAC TTAGATTGT TACCGAGTA GCAGTAGGAG CCGTGGCAGT

ecorV
3201 CCTGGATGC TTAGGCATA GGCTTGTGA TGCCGGTACT GCGGGCCTC TTGCGGATA TCGTCCATC CGACAGCATC GCCAGTCACT ATGGCGTGT
GGGACCTACG ACATCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AAGCCCTAT AGCAGGTAAG GCTGTCTAG CCGTCACTGA TACCGCACGA
3301

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FIG. 23E

> length: 3300

aatII (GACGTC):	1983
acc65I (GTACC):	795 1176
ageI (ACCGT):	1806 2126
ahaIII (TTTAAA):	590
ahdI (GACNNNGTC):	346 1495 2380
alw26I (CAGNNCTG):	1089 1770 2359
alw44I (GTGCAC):	1930 2169